

SPRING 2015

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HARVARD MEDICINE

THE
ADVENTURE
ISSUE

Brooks

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SPRING 2015 | VOLUME 88 | NUMBER 2

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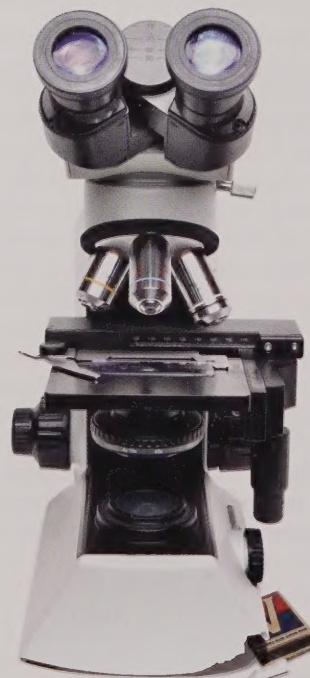
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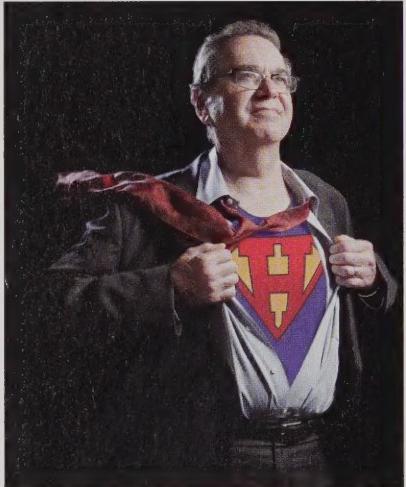
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From the Dean



I GREW UP DURING THE ERA OF SUPERMAN. Even though I wasn't a crazed collector of comics, or an avid fan of any one superhero, I loved the imaginative stories that involved powerful heroes. Those heroes were doing right for the world. I liked that.

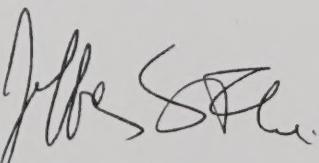
Having a deep-seated passion for doing something right for the world is fundamental to the work of our alumni and faculty. They do not shy from difficult questions or from knotty problems.

As this issue's cover makes clear, *Harvard Medicine* is celebrating the spirit of exploration and adventure by presenting stories of those who travel uncharted paths. These are tales of special people who, in the course of their everyday lives, do extraordinary things that in one way or another do right for the world.

Their adventures only occasionally happen at home. Researchers who search nature for new therapeutics or medical tools might start their explorations online but ultimately end up in a garden, on a seashore, or tramping through a tropical forest. Physicians might set up a practice, then find themselves working in the surgery of a nineteenth-century frigate or deep in the woods along the nation's northern border, using medical science to unlock the reasons behind unexplained deaths. Or home might be the place where an adventurer returns after a life-altering experience that involves nearly 2,800 miles and a grueling test of physical stamina.

We also look at some of the contributions that HMS researchers and clinicians are making in the fight against Ebola; we consider the state of research funding and its possible ramifications on the discovery pipeline; and we contemplate the importance of clinical trials that involve children—and the burden that consent decisions bring to those children and their parents.

Stories of engagement, stories of discovery, stories of adventure all come to you in this issue of *Harvard Medicine*.



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Harvard Medicine is published three times a year at 25 Shattuck Street, Boston, MA 02115.

Publishers: Harvard Medical Alumni Association and Harvard Medical School

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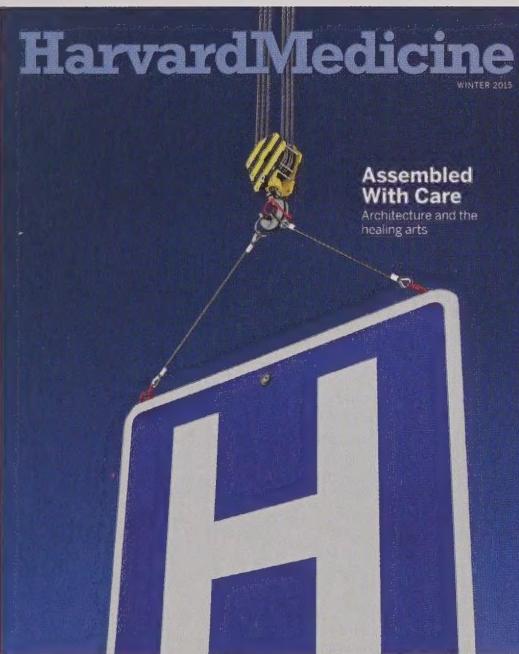
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ISSN 2152-9957 • Printed in the U.S.A.

Letters to the Editor

CHART NOTES FROM OUR READERS



In 1945, I was one of twelve women in my class. We were the first group of women to be admitted to the School, and it was evident that we were a new phenomenon.

RAQUEL COHEN '49
SURFSIDE, FLORIDA

One for the Books

David Cameron's engaging article, "On Speaking Terms" in the Summer 2014 issue of *Harvard Medicine* made it clear that although American English dialects are relatively homogeneous, there are still many words and phrases that can be problematic for physicians. Does "high blood" mean high blood pressure or high blood sugar? What does it mean to feel "donsie" or "pindling"?

If a young woman "falls off the roof," should you worry about a broken leg? How do you treat a "pumpknot" or a "runaround"?

As a result of this article, Douglas Kelling '72, and I have discussed stories of our encounters with regional medical language. We agree that a glossary of folk, regional, and old-fashioned terms for ailments, diseases, and body parts would be a useful resource for doctors who practice in a region other than the one in which they grew up. To that end, I am working toward the development of an application programming interface for the *Dictionary of American Regional English* (DARE), which would allow the creation of such an app for physicians.

While the information in DARE is wide-ranging, it is certainly not exhaustive. If readers of *Harvard Medicine* have examples of unfamiliar words they've encountered from patients, I would appreciate their passing them on to me for an eventual update of the DARE text and inclusion in a medical app. Please address correspondence to jdhall@wisc.edu.

JOAN HOUSTON HALL
CHIEF EDITOR
Dictionary of American Regional English
MADISON, WISCONSIN

Making Space

When I read "Structural Integrity" in the Winter 2015 issue of *Harvard Medicine*, I was surprised to learn that even as late as the 1970s, women were experiencing difficulties in their interactions with School faculty.

When I entered medical school in 1945, I was one of twelve women in my class. We were the first group of women to be admitted to the School, and it was evident that we were a new phenomenon. Although faculty members were helpful and polite, they were confused and really didn't know how to deal

with us. They often had lapses in recognizing a second gender in their midst. Most of the lectures in the first year, for example, began with the lecturer saying, "We will talk about this, gentlemen." Members of the faculty had a hard time adjusting their behavior.

In addition, there was no housing for us at Vanderbilt. I had studied at the School of Public Health before I entered HMS and had learned about a boarding house on Aspinwall Avenue. I told my female classmates about it, and six or seven of us lived there while in medical school.

The twelve of us in that first class were aware that it was a privilege to be admitted to HMS. I imagine that awareness still holds for today's students. I do wonder, however, whether the situation has improved for young women at HMS today.

RAQUEL COHEN '49
SURFSIDE, FLORIDA

Like Fine Wine

I found the "Second Opinions" article on end-of-life care in the Winter 2015 issue of *Harvard Medicine* to be a welcome discussion on the importance of listening and giving due to patients, regardless of age or infirmity.

My satisfaction with the piece and its content may have been heightened by my having recently read an article in which the author, a physician, said he'd prefer to die at age 75 than live to age 90. As an octogenarian, I was more than a little outraged; as a researcher who studies the facets of aging, I was disturbed; but as a physician and a member of society, I was disappointed. Once again, the entrenched concepts of aging were presented with fear and loathing.

When I was 57, I applied to the National Institute on Aging (NIA) for a grant that would support the Harvard Grant Study, part of the Study of Adult Development at HMS, an unprecedented longitudinal study that has followed a group of Harvard men from their undergraduate days in the late 1930s and early 1940s. The men were about 65 years old when I applied for the funding; I proposed charting their lives until their deaths. In my youthful ignorance, I believed that the men's fiery days were long over but that it would perhaps be instructive to watch the last of the flames peter out.

continued on page 4

When James Birren, then 78 and the chairman of the NIA, read my grant proposal, he became so inflamed by my ignorant ageism that he traveled from Washington to Boston to give me a severe, but generative, talking-to. He cured me of my age phobia and inspired what became my fascination with old age. How glad am I that Birren did not die at 75.

Thanks to his wisdom, I changed my focus, and the NIA funded the study for the next two decades. Today, more than 30 of the 268 men remain alive, each in his early to mid-nineties. And most are very glad to be so.

It was with some sympathy, then, that I read one man's argument for having his life end at 75. As I described in my 2012 book, *Triumphs of Experience*, the Harvard nonagenarians I have followed for nearly a half century have shown us how much we have to give even when we are no longer in what many consider our prime. Some study participants became guardians of the past as historians or genealogists. Some shared how their hard-earned experiences helped inform their roles as judges, mentors, and grandparents.

My worst fear when I applied for my grant—the toll of dementia—also has been informed by the evidence gathered in the study. It's true that, on their ninetieth birthdays, twenty-two of the seventy-seven surviving members of the Harvard Study had or would develop dementia. But just four years later, only four of the thirty-six men who survived have dementia. In other words, our study found that after age 90 the incidence of Alzheimer's disease decreased.

For most of us there does come a time when our worst fears about aging come true, but not, usually, until death is near. Yes, those final months are often excruciating and should not be elaborately prolonged. Yes, as the writers in "Second Opinions" state, our wishes for how those final months are lived should be talked about in advance of living them. Yes, the final months are costly, and their costs should be reduced. But death, and the expensive agony at its threshold, can happen at any time between birth and age 110.

In a *New Yorker* piece that appeared in 2014, Roger Angell, the 94-year-old sports writer and essayist, demonstrates old age's gifts of empathy and perspective. Without self-pity,

he first lists the physical insults of his aging: nerve pain from old shingles, a herniated disc, an angioplasty and "a couple of arterial stents," crippling arthritis in his left hand, a bad knee.

He then describes the real pain of old age, the kind that can't be relieved by any known medical intervention—having the loves in one's life die. He movingly describes some of these losses: his wife, a pain that still aches; his oldest daughter, the "oceanic force and mystery" of whose premature death, he writes, "had not left full space for tears"; his beloved terrier, Harry. "Why," Angell asks, "do [memories of them] sustain me so, cheer me up, remind me of life ... Why am I not endlessly grieving?" Perhaps it is because 90-year-olds are more resilient than the middle-aged. In Angell's words, "Surveys ... confirm that a majority of U.S. people over seventy-five keep surprising ourselves with happiness." Put me on that list.

I retired at 72 after turning the directorship of the Harvard Study over to a younger researcher. But I still tend to the study thirty hours a week. I remarried at age 76. Now 80, happily married, I hang out with my children and grandchildren. To my chagrin, I must admit that I may be more engaged with my children now than I was at the so-called height of my powers. It's true that I walk, talk, and think more slowly than I used to. I don't hike in the White Mountains anymore, and I've never used a smartphone. But I walk, I write. I'm not obsessed with staying young. Instead, I'm happy to be 80, and I look forward to turning 90. If arthritis and a dicey memory are the price I pay for the joy of attending my granddaughters' weddings, so be it.

GEORGE VAILLANT '59
ORANGE, CALIFORNIA

Sleep Over

I was most interested to read about the efforts to design more patient-friendly hospital rooms in "Better by Design," featured in the Winter 2015 issue of *Harvard Medicine*. It took me back to an in-hospital experience I had after open-heart surgery. In this advanced teaching hospital my bed was designed to squirm under me, presumably to help prevent bedsores. Subjectively, however, it was as though two incompatible anacondas were constantly wrestling under me. I wondered: What insensitive turkey had designed this torture device? I don't recall if I

avoided bedsores, but I certainly avoided sleep. After one night of this discomfort, I asked for relief, so the staff simply turned off the bed. It settled stably. Unfortunately, during my second night, the call-button control slipped off the bed and onto the floor. I was stuck: getting out of bed with a split sternum was both impossible and forbidden, and my piercing whistle did not carry through the hermetic door.

Feeling desperate, I hit upon an idea: I disconnected my chest monitor. This brought nurses rushing in. I explained my situation. With the call button more firmly anchored and the bed forced into quiescence, I finally slept.

THOMAS G. GUTHEIL '67
BOSTON, MASSACHUSETTS

A Special Everyman

I loved the overall theme of the Winter 2015 issue of *Harvard Medicine* and appreciated how the tribute to the work of Karl Wegner '58 ("Stately Renovation") was incorporated into it.

My husband, Karl, was proud to be a graduate of HMS and fully appreciated the top flight education given him as a result of his commitment to the Marine Corps from day one at Yale as well as from the "workingman" jobs he picked up during his years at Harvard, including pounding the pavement of Boston as a supplemental mail carrier and working as a night telephone operator at Harvard.

Under it all, Karl was always a boy from Pierre, South Dakota, the grandson of immigrants, which, summing it up, are reasons he was the perfect person to present his vision of a four-year, degree-granting medical school in South Dakota to our legislature—and get it accepted, passed, and implemented by all the powers necessary.

Thank you again for your tribute.
MARGARET WEGNER
SIOUX FALLS, SOUTH DAKOTA

Harvard Medicine welcomes letters to the editor. Please send letters by mail (Harvard Medicine, 107 Avenue Louis Pasteur, Suite 111, Boston, MA 02115); fax (617-432-0446); or email (harvardmedicine@hms.harvard.edu). Letters may be edited for length or clarity.



MAKE ME A MATCH

HMS students learn where their careers will begin

PHOTO FINISH: Adaugo Amobi celebrates the news of her residency match.

A bell rang, signaling to members of the class of 2015 that they could tear open the personalized envelopes containing news of where each would spend the next three to seven years of training.

On March 20, the annual Match Day ceremony, during which medical students learn where they will serve their residencies, was held at medical schools across the country.

Students who were candidates for matching, along with family and friends, assembled in the Tosteson Medical Education Center atrium to celebrate matches with hugs and high fives, selfies, and family photos.

Slightly more than 50 percent of matching students will spend part of their training in an HMS-affiliated program.

The nationwide match pairs students with residency programs around the country and is administered under the governance of the National Resident Matching Program, a nonprofit organization that helps provide an orderly and fair way to match applicants to U.S. residency positions.

Edward Hundert '84, the Daniel D. Federman, M.D. Professor in Residence of Global Health and Social Medicine and Medical Education and dean for medical education at HMS, noted that the students had worked hard to get to this point and that the road was not likely to get easier.

"The reward for a job well done is another job," he said at the ceremony.

Of the 161 students in the HMS class of 2015, 157 matched in clinical training programs and 4 are pursuing nonclinical positions. Slightly more than 50 percent of matching students will spend part of their training in an HMS-affiliated program.

This year, sixty-one HMS students matched in primary care specialties: forty in internal medicine, ten in pediatrics, five in obstetrics/gynecology, four in family medicine, and two in medicine/pediatrics.

One of the celebrants, Samsiya Ona, a Peabody Society member originally from Togo, matched to a joint program in obstetrics and gynecology at Brigham and Women's Hospital and Massachusetts General Hospital.

She hopes to focus on women's health, specializing on maternal-fetal medicine, and plans to split her time between Boston and Togo.

"I have two homes now," she said. "I can't deny it."

—Jake Miller

Big Bytes

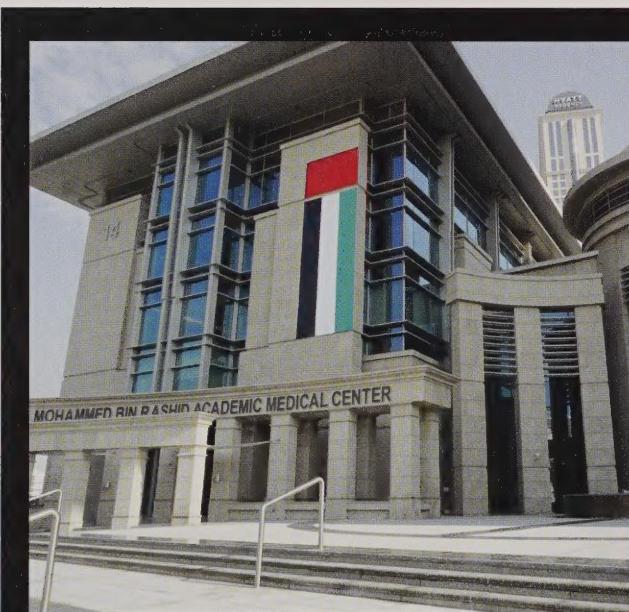
HMS welcomes new Department of Biomedical Informatics

EFFECTIVE JULY 1, HMS will add a new Quad-based department to its roster. The establishment of this new entity, the Department of Biomedical Informatics, will, according to HMS Dean Jeffrey S. Flier, emphasize the vital role the field of bioinformatics has at HMS and underscore the prominent role the School has played in the field's development throughout the past half century.

The department's inaugural chair will be Isaac Kohane, director of the Countway Library of Medicine, the HMS Lawrence J. Henderson Professor of Pediatrics at Boston Children's Hospital, and codirector of the Center for Biomedical Informatics (CBMI), the institutional predecessor to the new department. In 2014, CBMI, led by Kohane and Alexa McCray, an HMS associate professor of medicine at Beth Israel Deaconess Medical Center, brought in an array of federal grants that funded the establishment of large research collaborations among scientists on the Quad, at affiliated hospitals, and in the Harvard University Faculty of Arts and Sciences.

In his announcement, Flier explained why biomedical informatics is integral to contemporary medical research when he noted that "the field represents two converging communities: one involving health care-related data, and the other addressing the study of health and disease at molecular and naturally occurring systems level."

Mastering the surge in biomedical data streams goes beyond storage and computation. It includes developing and applying new methods for both research and clinical care. Central to the department's mission will be addressing methodological, engineering, and educational challenges. CBMI already has a strong history of education through its involvement in master's- and doctoral-level programs. The new department will continue to expand this commitment to education. It will launch with five core faculty members who are now associated with CBMI, and recruits will be added in the coming years to achieve representation from across the field.



HEALTH FOR ALL: The Mohammed Bin Rashid Academic Medical Center within Dubai Healthcare City is made up of a medical university, a medical library, and a medical simulation center.

Rashid Academic Medical Center in Dubai Healthcare City, a medical center campus.

Her Excellency Raja Al Gurg, vice-chairperson of Dubai Healthcare City Authority, attended the signing ceremony. "The work of the center," she said, "will support our long-term commitment to improving the health of all communities within Dubai and enhance our opportunities to lead the region in advancing health care research and delivery."

The new center will allow HMS, working with researchers and care providers from the health authorities in the UAE, to stimulate research and education aimed at improving health care capacity in such areas as surgical outcomes, treatments for diabetes and obesity, treatments for infectious diseases such as tuberculosis and hepatitis C, and mental health disorders.

The activities of the center also aim to strengthen the research environment in Dubai, the UAE, and the region and to contribute to regional social and economic development. The center will expand training capabilities for regional faculty and students but will not provide patient care.

—Stephanie Dutchen

Foundation of Care

New center in Dubai will focus on community health

A COOPERATIVE AGREEMENT signed in January by HMS and the Dubai Healthcare City Authority not only established the HMS Center for Global Health Delivery-Dubai but also signaled support for the center's mission: to increase local and regional health delivery research capacity, and, by extension, improve the health of the people living in Dubai and throughout the United Arab Emirates.

The new health research and training center will address some of the more pressing health challenges in Dubai and the region, expanding Dubai's role as a global hub for scientific and policy discussions related to health care deliv-

ery. Funding for the center will be provided by a four-year grant from the Dubai Harvard Foundation for Medical Research.

"We are privileged to partner with our colleagues in Dubai to generate best practices in global health delivery and to transform these practices into improved health outcomes in Dubai, the region, and the world," said Jeffrey S. Flier, HMS dean.

The new center, directed by Salmaan Keshavjee, an HMS associate professor of global health and social medicine and director of the Program in Infectious Disease and Social Change in the Department of Global Health and Social Medicine, will be based at the Mohammed Bin



BROWSER BEWARE

Concerns raised over online marketing of genetic tests for cancer

WEBSITES THAT MARKET personalized cancer care services often overemphasize benefits and downplay limitations. In addition, many sites offer genetic tests whose value for guiding cancer treatment has not been shown to be clinically useful.

According to a study reported by HMS researchers in the May issue of the *Journal of the National Cancer Institute*, the unregulated nature of online marketing of cancer-related genetic tests contributes to an unbalanced representation of the tests' benefits and limitations.

In their analysis of fifty-five websites offering these services, says first author Stacy Gray, "we found a lot of variation." In addition, 88 percent of the websites offered one or more nonstandard test that lacked evidence of clinical utility in routine oncology practice.

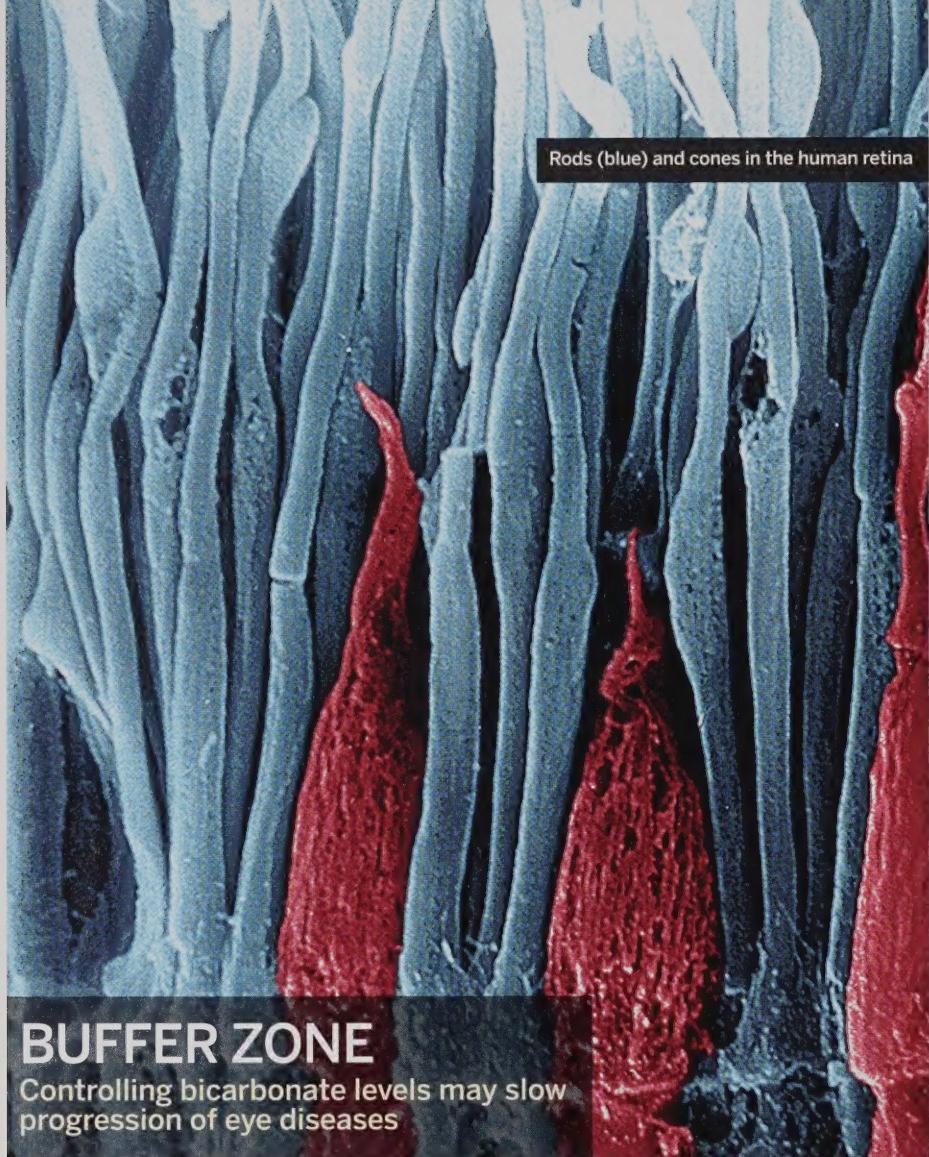
Gray, an HMS assistant professor of medicine at Dana-Farber Cancer Institute and an investigator in the Dana-Farber Center for Outcomes and Policy Research, was part of a team that included Katherine Janeway '00, an HMS assistant professor of pediatrics at Dana-Farber.

The investigators analyzed precision, or personalized, cancer medicine products and services marketed by such entities as private companies, academic medical centers, physicians, and research institutes.

Precision cancer medicine often refers to the testing of DNA from a patient's tumor to detect mutations or other genetic abnormalities that may help physicians predict how the disease will behave, and, in a limited but growing number of cases, in their selection of a therapeutic agent targeted to the particular mutations found. Such targeted agents may be more effective and cause fewer adverse effects than those used in standard chemotherapy.

More than 50 percent of the websites reviewed offered somatic testing, which is the genetic characterization of the tumor itself, while 20 percent marketed germline testing, which analyzes the patient's genome. Germline testing may identify altered genes that could indicate the risk of developing cancer. In addition, 44 percent of sites offered some form of personalized cancer care, with some claiming that their products led to treatments that increased life expectancies and others indicating that their analyses of tumors could identify effective treatments for a given cancer.

Claims and information posted on Internet sites are not regulated by agencies such as the U.S. Food and Drug Administration. The FDA recently indicated, however, that it intends to begin regulating genomic testing more broadly.



BUFFER ZONE

Controlling bicarbonate levels may slow progression of eye diseases

BICARBONATE, an important naturally occurring compound in the body, plays essential roles in buffering pH, aiding in digestion, and neutralizing lactic acid produced during physical exertion. Much of the bicarbonate in our bodies comes from carbon dioxide that is produced as waste in all cells as well as from that ingested with certain foods and beverages.

Now, a study led by HMS researchers in the Makino Laboratory at Massachusetts Eye and Ear reports that bicarbonate also alters how we see: It modifies the visual signal generated by specialized retinal cells that detect light. The study appeared online March 12 in the *Journal of Biological Chemistry*.

Within those specialized cells, known as rod and cone photoreceptors, a soluble molecule called cGMP links photon absorption to the electrical activity of a photoreceptor. When it is exposed to light, cGMP is destroyed and ion channels are closed. Positively charged sodium ions cease to enter the rod or cone, and the membrane potential becomes more negative or hyperpolarized. Bicarbonate helps photoreceptors recover from the loss of cGMP by stimulating guanylate cyclase, an enzyme key to the synthesis of cGMP.

"By opposing the effect of light, bicarbonate limits the size of the photon response and quickens its recovery," says lead author Clint Makino, an HMS associate professor of oph-

thalmology at Mass Eye and Ear and director of the Makino Laboratory. "As a result, sensitivity to light is slightly lower, but our ability to track moving objects is improved. An intriguing implication is that vision may change with metabolic state, although further research is necessary to confirm this."

"It is now known," he adds, "that in some types of retinal diseases, a genetic defect causes cGMP in the rods and cones to rise to lethal levels. Once lost, rods and cones are not replaced, leading to irreversible blindness."

Scientists in the Makino Laboratory want to investigate the possibility that controlling bicarbonate levels in the eye will slow the progress of, or even prevent, eye diseases. —*Mary Leach*

Medical Bliss

Physicians less likely than other health professionals to divorce

THE LARGEST INVESTIGATION of divorce rates among physicians has resulted in a finding that may surprise many: Physicians are less likely to divorce than are people in other occupations, including lawyers and other health care professionals.

The study, published online February 18 in *BMJ*, did find, however, that female physicians who worked longer hours had a greater likelihood of divorce than did male physicians.

"It's been speculated that doctors are more likely to be divorced, but no large-scale study has ever investigated whether that is true," says Anupam Jena, an HMS assistant professor of health care policy at Massachusetts General Hospital and senior author of the report.

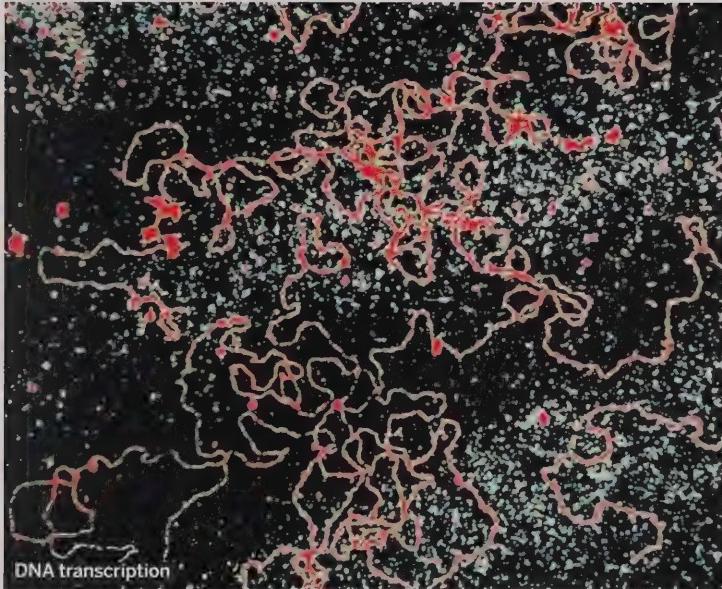
Previous studies finding higher divorce rates among physicians depended on small, nonrepresentative samples, some from a single institutions, the authors note. Those studies were published three or more decades ago. To get a more comparative and contemporary picture of the divorce rate among physicians, the researchers analyzed data from an annual survey of around three million households conducted by the U.S. Census Bureau.

Survey results from 2008 through 2013 included responses from approximately 200,000 health professionals, including more than 48,000 physicians. Although 24 percent of physician respondents had a probability of ever being divorced, the probability of being divorced was 25 percent among dentists and 33 percent among nurses. Only pharmacists, at 23 percent, were less likely than physicians to have been divorced.

Female physicians were approximately one-and-a-half times more likely to be divorced than male physicians of a similar age. Female physicians who reported working more than forty hours per week had a higher probability of being divorced than those working fewer hours. The apparent impact of hours worked on divorce incidence was the opposite for males.

—*Sue McGreevey*





The Long and the Short of It

Mutations in a single gene may spur Rett syndrome

FOR FIFTEEN YEARS, SCIENTISTS HAVE KNOWN that mutations in a single gene, MECP2, lead to Rett syndrome, a severe neurological disorder that affects young girls almost exclusively. Even so, they have struggled to understand how the gene functions in the brain in Rett syndrome.

An HMS research team now has discovered that when MECP2 is mutated in a mouse model of Rett syndrome, the brain loses its ability to regulate unusually long genes. Their finding suggests new ways to consider reversing the intellectual and physical debilitation this disruption causes with a drug that could potentially target this error. The team, led by Michael Greenberg, the Nathan Marsh Pusey Professor of Neurobiology at HMS, reported its findings in the March 11 online edition of *Nature*.

Scientists, including Greenberg, have learned that MECP2 plays a role in sculpting the connections between neurons in the developing brain. These synapses mature as they are exposed to sensory experiences, just the sort of stimulation a young child would encounter as she learns to walk and talk.

MECP2 is present in all cells in the body, but when the brain is forming and its synapses are maturing, MECP2 levels in the brain are nearly ten times higher than in other parts of the body. The Greenberg study links MECP2 mutations to long genes, which may be more prone to errors simply because their length leaves more room for mistakes.

"MECP2 may act like a speed bump, fine-tuning long genes by slowing down the machinery that transcribes them," says Harrison Gabel, a post-doctoral fellow in Greenberg's lab and co-first author. In transcription, the information in a strand of DNA is copied onto a new molecule of messenger RNA, which is then turned into a protein. Without MECP2, transcription may move too fast, leading to widespread overexpression of the long genes.

Harrison and co-first author Benyam Kinde, an MD-PhD student in Greenberg's lab, found the misregulation in multiple mouse models of Rett syndrome and confirmed it in the brain tissue of deceased Rett patients.

As an attempt at a corrective strategy, the researchers chose the cancer drug topotecan because it blocks an enzyme known to be important for long-gene transcription. When they added topotecan to neurons lacking MECP2, the drug reversed the long-gene misregulation. Although topotecan is too toxic to be a therapeutic, derivatives of topotecan might prove worthwhile.

—Elizabeth Cooney

Between the Lines

Model indicates pseudogenes may lead to disease development in humans

PSEUDOGENES have long been considered to be genomic junk. A subclass of long noncoding RNA, these entities developed from the human genome's 20,000 protein-coding genes but lost the ability to produce proteins. Yet the retention of these remnants throughout evolution suggests that they may have biological functions.

A research team at HMS and the Cancer Center at Beth Israel Deaconess Medical Center has provided some of the first evidence that one of these noncoding evolutionary relics has a role in causing cancer.

In a study published April 19 in *Cell*, the scientists report that, independent of any other mutations, abnormal amounts of the *BRAF* pseudogene led to the development of an aggressive lymphoma-like disease in a mouse model, a discovery suggesting that pseudogenes may play a primary role in a variety of diseases.

The discovery of this activity by pseudogenes also suggests that the functional genome could be three or four times its current known size.

"Our mouse model of the *BRAF* pseudogene developed cancer rapidly and aggressively," says senior author Pier Paolo Pandolfi, the HMS George C. Reisman Professor of Medicine at Beth Israel Deaconess. "It's remarkable that this very aggressive phenotype, resembling human diffuse large B-cell lymphoma, was driven by a piece of so-called junk RNA."

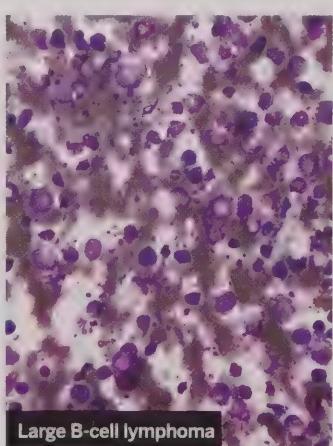
The discovery hinges on the concept of competing endogenous RNAs (ceRNA), a functional capability for pseudogenes in which noncoding RNAs divert and sequester tiny pieces of RNA from their protein-coding counterparts so as to regulate gene expression.

The scientists wanted to determine whether this same ceRNA "cross talk" took place in a living organism with similar consequences.

The investigators focused on the *BRAF* pseudogene because it is known to exist in both humans and mice. The team created a mouse model in which the *BRAF* pseudogene was overexpressed and found that the mice overexpressing the pseudogene had higher levels of the *BRAF* protein and hyperactivation of a cancer-related pathway.

The investigators also found that the *BRAF* pseudogene is overexpressed in human B-cell lymphomas and that the genomic region containing the *BRAF* pseudogene is amplified in a variety of human cancers. Moreover, the authors say that silencing overexpressions of the *BRAF* pseudogene in human cancer cell lines led to reduced cell proliferation. This suggests that a therapy that reduces *BRAF* pseudogene levels may benefit cancer patients.

—Bonnie Prescott



Large B-cell lymphoma



Listen Up

The brains of preterm newborns can reshape in response to the familiar—their mother's voice

NEWBORN BABIES' BRAINS develop rapidly in response to sensory stimuli, and even though they have been found to respond to their mother's voice and heartbeat before birth, little has been known about how and to what extent this prenatal auditory stimulation shapes the brain.

Now, a study by HMS researchers shows that the human brain is capable of forming neural connections in response to maternal stimuli even at a very early gestational age. Amir Lahav, an HMS assistant professor of pediatrics, is senior author of the paper, published in the January issue of the *Proceedings of the National Academy of Sciences*.

The researchers set out to determine whether enriching the environment of prematurely born infants with sounds that mimicked what a full-term baby would have "heard" in the womb would result in structural changes in the auditory cortex.

Forty extremely premature infants (25 to 30 weeks' gestation) in the newborn intensive care unit at Brigham and Women's Hospital were randomized into two groups. Twenty-one of the infants were exposed inside their incubators to low-frequency recordings of their own mother's voice and heartbeat, similar to what a baby would hear in the womb, for three hours each day. Nineteen other infants, the control group, were exposed to the noises commonly occurring in the NICU. After about 30 days, the researchers used cranial ultrasonography to determine the size of each infant's auditory cortex. They found that the auditory cortices of infants in the maternal sound group were sig-

nificantly larger compared with those of infants in the control group.

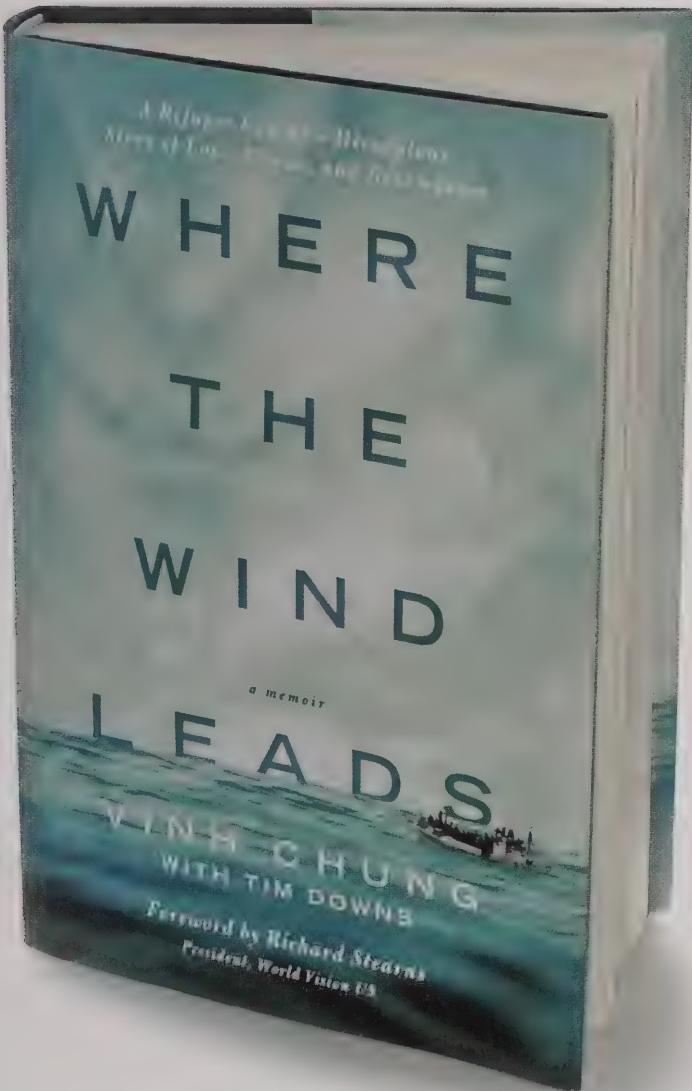
The authors suggest that the high plasticity of the auditory cortex in response to maternal sounds at this critical prenatal stage might provide the "auditory fitness" necessary to help shape postnatal brain development, somewhat akin to priming a pump. In addition, recorded maternal sounds may be especially helpful for medically fragile premature babies, whose exposure to live maternal stimulation is often limited because the infants spend so little time outside the incubators.

The authors note that although exposing preterm infants to biologically authentic recordings of their mother's voice and heartbeat does not begin to address all the challenges facing these babies, it could negate some of the deleterious environmental effects of the NICU and, potentially, ready the brain for hearing and language development.

—Susan Karcz

BOOKMARKS

REVIEWING THE WRITTEN WORD



TRUE BEARING

Where the Wind Leads: A Refugee Family's Miraculous Story of Loss, Rescue, and Redemption
by Vinh Chung with Tim Downs
(W PUBLISHING GROUP/THOMAS NELSON, 2014)

reviewed by Elissa Ely

Where the Wind Leads looks backward. That's what a memoir does. It's about traumas unfathomable, and how Vinh Chung '04 and his family rallied to face the impossible. It is not, thank goodness, about becoming a doctor, which is another excellent reason to read it.

Chung was "born in a country that no longer exists and grew up in a country I never knew existed." His family thrived in South Vietnam; quiet capitalists who ran a rice-milling business named Peace, Unity, Profit. The business was overseen by his widowed grandmother, an operational genius who had "a temper like a Laotian land mine" and "opened Pepsi bottles with her teeth." The extended family lived in a French colonial, and the children were driven to school in a Mercedes.

After Saigon crumbled in 1975, the mill was reassessed as a governmental treasure and permanently "borrowed" by the People's Army. So were the car and the house. Under the new regime, old money was just paper, burned as fuel to cook pig food.

Vinh was three and a half years old when his family—and 280 unrelated others—set sail in a seventy-foot boat without bathrooms after bribing the government to wink at their departure. Family jewels were smuggled in diapers, money was sewn into pants hems. There was no destination.

This trip is futile to imagine by those of us who, at the time, were students moving within the cosmos of Buildings A, B, C, and D. At HMS, we were rotating stereoisomers while pirates off the coast of Malaysia were ramming the refugees' wooden boat. While children were dropped over the hull into their fathers' arms and carried through the sea onto Malaysia's shore

(Vinh's first memory), we were plating petri dishes. Bacterial colonies grew out in colors while the unwelcome refugees were forced back to sea in smaller boats without tillers, water, or food.

Finally, the refugees were discovered by a Christian rescue freighter, deliberately trolling the South China Sea. Neither rescuers nor rescued felt that the discovery was random. In the midst of 600 miles of ocean, they took it as a purposeful miracle. In Boston, we took finals.

The final third of the book follows the family's first years in the United States: Arkansas, of all places, where "all Caucasians ... look the same to Asians." The family enlarged to eleven, and the youngest children learned to speak Vietnamese in their Baptist church. For the kids, life was full of Americana: Halloween, football, math exams. They grew up to become teachers, researchers, dentists, and doctors. For the parents, life was different. Chung's father, the former COO of a multimillion dollar enterprise, worked an assembly line. Chung's mother cooked in a Chinese restaurant.

This is a memoir in which the author frankly acknowledges his multiple sources. To be one hundred percent accurate (and, as a Mohs surgeon, I'm sure he is), Chung was too young to recall most of his life in Vietnam. But he can and does piercingly recall the existence that all refugees face until they find home: "no nation mourned their departure, none awaited their arrival ... there was heartbreak but not history ... [for refugees] were just some country's former problem."

Elissa Ely '87 is a psychiatrist at the Massachusetts Mental Health Center.





Looking to nature for inspiration
allows researchers to think outside
the lab by Stephanie Dutchen

INTO THE WOODS

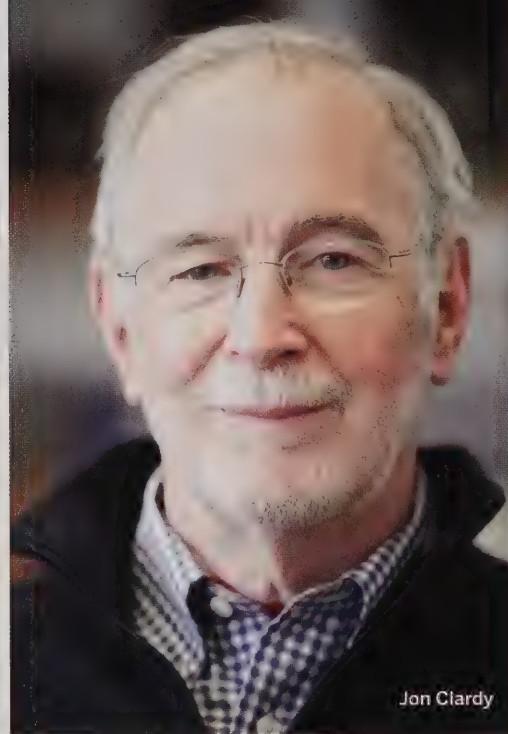
Joanna Aizenberg discovers that a butterfly's wings change color when exposed to liquids other than water and considers how she can integrate that color-tuning property into noninvasive diagnostic devices. ■ Jeffrey Karp wanders through a cactus garden in Arizona, gauging whether the barbs at the ends of the plants' delicate spines could inspire improvements in surgical tools. ■ Jon Clardy heaves aside a shovelful of soil in the Atlantic Forest of Brazil, hoping the bacteria in the ant nest he's

unearthing will lead to a treatment for invasive fungal infections.

■ For all three researchers, looking to nature inspires unconventional solutions to biomedical problems. Key to their success is an adventurous spirit and an eagerness to veer off the beaten track, literally and conceptually. ■ “There are many systems I study in nature that nobody has looked at,” says Aizenberg, the Amy Smith Berylson Professor of Materials Science in Harvard University’s School of Engineering and Applied Sciences and leader of the adaptive material technologies platform at the Wyss Institute for Biologically Inspired Engineering at Harvard.



Joanna Aizenberg



Jon Clardy



Trying to translate the stickiness of a gecko's foot into a medical adhesive, as Karp has done, or to find a microbial compound that fights cancer, as Clardy has done, is risky: The likelihood of failure is high, funding is harder than usual to secure, and the path to a result isn't clear. Even when an effort yields a radical advance, the discovery can be met with resistance.

Some people are frightened by all that uncertainty. But natural product hunters and bio-inspired engineers are driven by it.

Nothing Ventured, Nothing Gained

"There's adrenaline in this kind of work, but it's not from fear," says Clardy, the Hsien Wu and Daisy Yen Wu Professor of Biological Chemistry and Molecular Pharmacology at HMS. "There's excitement about what you're going to find, what's going to be different today from yesterday."

Whether they're sampling life forms in far-flung environments or poring over PubMed for ideas, biomedical scientists who explore nature for their inspirations share traits with classic adventurers.

"We're all equipped with certain tools or skills, we're advancing with a certain level of confidence that we can make it pretty far, with the belief that we can achieve something new," says Karp, an HMS associate professor of medicine at Brigham and Women's Hospital. "But we really never know what's around the corner."

"Those who fear the unknown have a difficult time," he adds. "You have to take all the information you've learned, all the skills you've acquired, and just leap—and hope for the best."

These intrepid sorts don't always land on solid ground. But when they do, they change medicine.

The Great Outdoors

"Look outside," says Karp. "Every animal, every plant, every living thing has overcome an enormous number of challenges and is full of solutions."

Sometimes, capturing those solutions for medicine appears straightforward. Poppy plant extracts become opium and then morphine. Brazilian arrowhead viper venom leads to the first ACE inhibitor.

Most of the time, however, says Karp, "You can't just scrape something off a tree or the bottom of the ocean to solve a medical problem of interest. You need to go beyond nature."

Researchers like Karp and Aizenberg, who practice bio-inspired engineering rather than biomimicry, aren't trying to improve upon nature; they're inviting nature to collaborate or even to be their mentor.

A plant or animal with an intriguing property likely developed it for a different reason, in a different environment, and with materials different from those that would be optimal for medicine. By examining, adapting, and combining those properties, bio-inspired engineers extract new concepts from some of the world's oldest innovations and devise technologies that produce medical solutions that are effective, stable, scalable, safe, and, not least, customized for use in the human body.

Thief of Nature

When Karp set out to develop a glue that would help surgeons repair septal defects in beating hearts, the criteria were daunting. He knew of materials that would suit the elasticity, biocompatibility, and biodegradability requirements, but he was less sure about the

characteristics needed to make something stick in the presence of flowing blood.

So he asked nature, via Google.

He read studies of creatures that exist in wet, dynamic environments, eventually homing in on slugs, snails, and marine sandcastle worms. He learned that their viscous secretions contain hydrophobic agents that resist flowing water.

Attempts by others to develop tissue glue had focused on hydrophilic agents. Karp bet on the slugs and went hydrophobic.

The gamble paid off. The glue repelled blood and held repair patches in place. He made a version that activated with light so surgeons could cure the adhesive on command.

Similar methods have led Karp to develop medical devices that echo characteristics of jellyfish tentacles, porcupine quills, parasitic worms, and spider webs.

Walk on the Wild Side

The glow in a dark corner of a rock shop caught her eye.

While browsing for some shells, Aizenberg followed that glow to its source. It was the exoskeleton of a sea sponge. Turning the pale, webbed tube in her hands, she marveled at how the structure exhibited both strength and luminescence.

Years later, after launching investigations to understand, manipulate, and ultimately exploit the sponge's unusual characteristics, Aizenberg still appreciates its multifunctionality. She's fascinated by organisms that have evolved to solve multiple challenges with a single material. She also thinks the best way to adapt organic solutions for



Jeffrey Karp

human benefit is to combine properties from many sources.

Aizenberg has created water- and ice-deflecting surfaces that borrow ideas from water strider legs, mosquito eyes, and leaf bristles. The butterfly-inspired color-changing technology, called W-Ink, also owes a debt to beetles and brittlestars. In developing a highly frictionless surface called SLIPS, short for slippery liquid-infused porous surfaces, she took her cue from pitcher plants. A follow-on technology called tethered-liquid perfluorocarbon, or TLP, incorporates self-lubricating features inspired by intestinal mucus and the film that moisturizes our eyes when we blink.

Aizenberg's goal is to get to the bottom of how each sought-after trait works. Her only limitations: what today's technology can probe and what is known about the trait's evolutionary benefit to the organism. Once Aizenberg understands a system, she can play with it.

"I can rationally design it, customize its components, and adjust for what is specific to a particular application," she explains.

Currently, she has a handful of bio-inspired technologies that can be applied to fields ranging from optics to transportation to building materials to medicine. Coating medical tubing and catheters with SLIPS and TLP, for example, may prevent the formation of blood clots and biofilms.

As they search for new solutions to medical problems, Karp, Aizenberg, and Clardy must think orthogonally. They also must forge their own paths.

Off the Beaten Path

Do these quests for the undiscovered make them modern-day David Livingstones,

hacking through jungle until they come upon the biomedical equivalent of Victoria Falls?

"Livingstone and his guides at least knew there was a lake here, a river there," says Clardy. "We know so little about microbial ecology. It's more like exploring Mars."

Antibiotic discovery has slowed in recent decades in part because people keep sampling the same kinds of soil and rediscovering the same compounds. Clardy charts new territory by collecting samples from unexplored or underexplored ecosystems. When he does decide to probe that tired soil, it's because he's developed new biochemical techniques to culture bacteria species that have not yet been cultured, ones that have slipped through other scientists' fingers.

Aizenberg also prefers to strike out into untrodden areas; she avoids investigating materials that obsess others in her field.

"Pretty much everyone who's talking about developing tough materials is talking about mollusk shells," she says. "After hundreds of years of research, nobody can replicate that structure. Enough mollusk shells! I want to look for interesting things that others haven't studied, hidden clues that others haven't paid attention to."

Deciding against what Karp calls the "boring linear path" makes the work of these researchers more thrilling—and fulfilling.

"Of course, one can do science by clearly defining the goals and expected outcomes," says Aizenberg. "But to me that would be boring. When we cannot do something, or the results are absolutely opposite what we expected, then I'm interested. That is an adventure. That's risk taking. It's going after serendipitous results."

This penchant for the path less traveled can have consequences. Aizenberg readily admits her lab publishes less often than others do, opting instead for high impact over frequency. That can not only drive away young researchers, it can place her further from the money.

"The Indiana Jones sort of adventurer doesn't fare well in the current funding atmosphere," says Clardy.

But taking risks isn't the same as recklessness. Clardy, Karp, and Aizenberg make educated guesses about where to look for answers. They build on the work of others. They diversify, knowing not everything will pan out. When Karp and Aizenberg translate natural phenomena into medical devices, they use materials already proven safe in humans. That adds up to a project

success rate as high as 50 percent, Aizenberg says.

Still, they're accustomed to side-eyeing from fellow scientists. Natural product hunting is viewed as offbeat these days, Clardy says. "People used to think I was crazy. They probably still do."

Their Moments of Zen

Clardy has gone scuba diving for soft corals near mangrove swamps and in the Caribbean Sea. He's tramped through Costa Rican forests. This summer, he's heading to Brazil.

He won't regale you with tales of glamorous exploits, though. To hear him tell it, the corals were "slimy, mucus-producing things." Digging near the equator was hot, sweaty work, and he had to tape his pants to his boots to keep bugs out. "The whole thing is really kind of grim," he says.

And yet, "I'd rather be out digging ant nests than sitting in Boston in a snowstorm."

That's not only because of the weather. Changing venues changes his routine, which, in turn, can change his way of thinking. Fieldwork also separates him from his electronic devices for most of the day. It has, he says, a contemplative aspect that he enjoys.

The same holds true for Aizenberg, who has been known to spend hours on the beach gazing at the patterns that retreating waves carve in the sand, pondering the complexities of self-assembly.

There and Back Again

At the beginning of *The Hobbit*, Bilbo Baggins tells the wizard Gandalf, "Sorry! I don't want any adventures, thank you. Not today!"

He then spends three hundred pages going on a quest with dwarves, getting captured, riddling with strange creatures, and fighting a dragon. But after it all, he's happy to go home.

Like Bilbo, Clardy, Aizenberg, and Karp are homebodies at heart. They love bench science. Inspiration, after all, can also be found on the computer, at the city zoo, or in the garden.

Karp recalls brainstorming with lab colleagues about animals that "stick into things": bees, mosquitoes, porcupines. One thing led to another. Now surgical staples inspired by porcupine quills are moving toward large animal studies and, perhaps, to clinical trials.

"And that adventure," he says, "started right in this office." ■

Stephanie Dutchen is a science writer in the HMS Office of Communications and External Relations.



BREATHTAKING: Views of the terrain in Canada's Banff National Forest hint at the physical challenges facing those riding in the Tour Divide.



BIKING WITH WOLVES

A physician searches for the elemental truths of body and mind by Nathaniel Cobb





The Great Divide in North America is a geographic concept that has always intrigued me. It is the high and lonely spine of the continent, the hydrologic break that separates great rivers and the oceans they feed. Winters are long there, summers brief and exuberant. I have lived close to the Divide—and to its metaphors—for most of my life, and I never cross it without some inner genuflection. Must I choose one side over the other, one watershed, one fierce vector for my whole life? Why not straddle the Divide, watching the water flow down each side in turn, while staying as far as possible from sea level and the lowland masses?

I had the chance to live those questions during the summer of 2014, when I participated in a bike race called the Tour Divide. That adventure began in early June.

June 17: South of Bigfork, Montana. It has rained and snowed much of the time for four days now, and I wish it would stop. Instead of camping, I stayed in a motel last night to dry out my kit and prepare for another early start. The only food available late in the evening was pizza, which did not meet my criteria for “good fuel,” but I forced myself to eat slice after slice. This morning, nothing is open at 5 a.m. except a coffee shop, so I start out with just coffee and a piece of pie. Grinding up a 2,000-foot climb in steady cold rain I am warm enough, but flying down the other side, I become really cold. My gloves are soaked from the water running down my sleeves, and my toes are a distant memory. Somehow, I left my wool hat drying in the hotel bathroom. Because of my detour into Bigfork, I have to subtract 6 miles from the bike odometer to place myself accurately on the map, and I can’t do the math. Stopping under a larch to put on more clothes, my heavy bike tips over and the can of bear repellent spray falls out, enveloping me and my bike in a reddish cloud of aerosolized Tabasco. Good thing I’m from New Mexico. I smile. The humor, and the burning, clear my hypothermic haze. The map makes sense to me now.

Divide and Conquer

The world’s hardest bike race is not the Tour de France; it is the Tour Divide, a mountain-bike route of more than 2,700 miles that runs from Banff, Alberta, Canada, to Antelope Wells, New Mexico. The route crosses the Continental Divide thirty-two times, rising 200,000 vertical feet along the way.

The route didn’t start as a course for a race. In the late 1990s, the Adventure Cycling Association published a map of the route. Some bikepackers rode it, and one of them set out to see how quickly he could finish it. The next year someone beat his time.

The friendly competition evolved into a race with one stage, no entry fees, no permits, no support, and no organizing or sanctioning body; just an informal gathering in Banff at 8 a.m. on the second Friday in June before riders start out on the Great Divide route to New Mexico. A rider can use only the resources that he or she can carry or that are available to all, such as restaurants, hotels, bike shops, and convenience stores. A rider also can accept the kindness of strangers, known as “trail magic,” as long as the generosity is genuinely spontaneous. Each rider carries what is called a spot tracker, which sends location



PIE AND BIG SKY: When Nathaniel Cobb refueled at a restaurant in Pie Town, New Mexico, he was near the end of the tour route and nearing the end of his endurance, but not his commitment to completing the race.



Wind River Range in Wyoming

coordinates every ten minutes to a satellite and has an SOS function that will summon rescuers. The tracker transforms a rather lonely ride into a spectator sport, as family and friends follow the silent dots along a map and speculate about what their rider is feeling.

June 25: Pinedale, Wyoming. It was a spectacular ride today over Union Pass. I saw a grizzly across the meadow where both of us were having a snack. I waved and greeted him, but he was busy with his fish and wasn't interested in me. Then came a long, difficult downhill section with washboards, washouts, and loose rocks, followed by a couple of hours of smoother gravel and then paved road.

For several hours today I enjoyed the company of another racer. Human contact is precious in this empty country, and we pilgrims quickly shared our stories with one another.

My knees are really hurting today; they seem to be getting worse, and both Achilles tendons are swollen and creaking with every pedal stroke. Pushing my bike uphill through the snow in stiff cycling shoes has not been good, and it feels like the constant cold and wet have turned my synovial fluid to sludge. By the time I get to Pinedale, I am really worried that my joints won't make it for another 1,600 miles, so I stop in a pharmacy and pick up some anti-inflammatory drugs. My camp that night is next to an overhanging rock along the Emigrant Trail, on sweet-smelling

earth in the sage and aspen. The Milky Way is a phosphorescent wave breaking above me. At this moment, there is no place I'd rather be.

Watersheds

I was born in 1950, the dividing point of the twentieth century. In that year the population of the United States reached 150 million. Growing up in New Mexico and Colorado gave me a taste for wide-open spaces and high altitudes, and I spent a decade as an Outward Bound instructor and guide on the rivers and mountains of that glorious country. In my thirtieth year I crossed over a high pass and began an entirely new adventure as a first-year at HMS. The physical challenges were different but the intellectual journey was definitely in nosebleed country, yet I felt that, in some unusual way, I was well prepared for the challenge. After all, I had been living and breathing the Outward

Bound philosophy, which, as summarized by its founder Kurt Hahn, is to impel people into value-forming experiences and to ensure the survival of enterprising curiosity, indefatigable spirit, tenacity in pursuit, readiness for sensible self-denial, and, above all, compassion.

Aren't those exactly the qualities that make a successful medical student and a good doctor? I was indeed reasonably successful that first year, thanks in part to the pass-fail system, and to having discovered a kindred spirit reading a climbing magazine in the back row of Amphitheater C. I shared with Fred St. Goar '84 my dream of sea kayaking in the Northwest. The following summer Fred and I, with classmates Jeff Berman '84 and John Stogin '84, and friends Kim Howard and Sarah Wheeler (now my wife), undertook a six-week paddle up the wild Pacific coastline of Southeast Alaska. It was my considered



FIELD OF DREAMS: One of many evenings under the stars was spent in a stand of trees south of Steamboat Springs, Colorado.



PILGRIM'S PROGRESS: The landscape of New Mexico welcomed Nathaniel Cobb to his home state and to the race's end in Antelope Wells.

intent to maintain contact with the important threads of my past life in boots and boats while starting my new career in white coat and with stethoscope.

Thirty years and a hundred adventures later, I retired from work at the Centers for Disease Control and Prevention and the Indian Health Service. The years had introduced two stents in my coronary arteries and a growing obsession with the Continental Divide. I was in the mood for something solitary and epic, a journey into my own mind using this aging body, which seemed different every day. The Tour Divide became my pilgrimage, a chance to touch the holy places and inhale their power.

Taking Stock

I took a year to prepare. Putting the bike and equipment together was the best part: the perfect excuse to buy new gear! I pored over specification sheets and catalogs and considered the tradeoffs between durability and mass for each part. I calculated the incremental energy required to move an extra 500 grams up the estimated 60,000 meters to be climbed throughout the course and resolved to carry only what was necessary.

Getting my then 63-year-old body ready was not so much fun. I hired a personal trainer to help me develop the core and upper body strength I would need to keep my back healthy and a cycling coach to help me build the endurance my legs would need to ride more than 100 mountainous miles a day. I made field trips to convenience stores and reported my choices to a nutritionist, who then advised me on ways to optimize my food intake for long days in the



saddle. After an intense discussion with my cardiologist about the relative risk of a stent thrombosis versus bleeding into a head injury, we agreed that I would stop taking Effient and instead take an aspirin and a statin every day.

"You have to live your life," he said, "and do the things that make you feel fulfilled. Living in fear won't work for you. Just be smart and listen to your body."

July 7: Gila National Forest, New Mexico. Since leaving Pie Town yesterday afternoon, it feels like my legs just won't work. The bruises on my sit bones are amazingly painful, but I don't have the leg strength to stand on the pedals. I stop at a small waterfall to cool off and hydrate, I take electrolyte pills, I eat more food, I take Tylenol and Naprosyn. None of this helps. The endless succession of thousand-foot climbs on rough roads in the dust and the heat is really getting me down. I'm surprised, because I know this area, and I am getting close to the finish.

I try to diagnose myself. Could I be out of calories or dehydrated? I stop to eat and drink again and again, to no avail. Maybe electrolytes? Magnesium? I wish I could run my chemistries. Surely something is totally out of whack. Must be my thyroid. Should I take an extra dose of Synthroid? My left quad is really tender, possibly an isolated rhabdomyolysis from the statin. I wish I had some caffeine or coca leaves.

It's almost dark, and I stop by a tiny stream to filter drinking water and make a meal of my remaining scraps of food: potato buds, protein powder, and sardines. I ride on into the night, and somehow the dark and the coolness help. I am able to crest one more hill to camp by the Continental Divide sign. I think about the Outward Bound philosophy, and it seems that the only arrow left in my quiver is "tenacity in pursuit," but that one is sufficient. It is still 50 tough miles to the next meal in Silver City, but I have crossed an emotional divide. I make it there by 10 a.m. for a fabulous breakfast. I roll the last 125 miles through the magnificent desert in the twilight, with thunderstorms all around, and make it to Antelope Wells at noon the next day—2,752 miles in 26 days, 4 hours, and 15 minutes.

Trail Wisdom

People ask me, "What did you think about while you were riding?" Really, I didn't do a lot of thinking. Most of the time I just counted pedal strokes or breaths—one-and-two-and-three-and-four—or noticed a wildflower, the smell of sage after rain, or simply the vastness. Or I reminded myself that the experience of pain does not have to lead to the mental construct of suffering. Before the ride I visualized how I would focus on three simple concepts: the physical body, the wilderness, and the mental qualities of knowledge, skill, and tenacity. The ride was to weave these threads into a braid of wisdom that I could show others and be comforted by. After Antelope Wells, however, it's not that clear. Looking back, the only thing that was simple was the trail, first on one side, then on the other, of the Great Divide. ■

Nathaniel Cobb '84 lives in New Mexico. He participated in the Tour Divide ride as a fund-raiser for WildEarth Guardians, a group that seeks to preserve wildlife habitats, such as those important to wolves.



Michele Felice Corné
In Action

Action between USS Constitution
and HMS Guerriere, 19 August 1812

32 x 48 inches

Oil on canvas

In the collections of the
U.S. Naval Academy Museum,
transferred from the Navy
Department in 1869.



OFFICIAL U.S. NAVY PHOTOGRAPH

During conflict and calm, Amos Evans cared for the crew of Old Ironsides
by Louis Norton

High Seas Surgeon

AT THE TIME the United States declared war on Britain on June 18, 1812, vessels in the U.S. naval fleet were authorized to carry one surgeon and one or two surgeon's mates.

One of those surgeons was Amos Evans, Class of 1814.

Evans was assigned to the frigate *Constitution* early in 1812. At the time, his medical training was rudimentary, consisting of a three-year apprenticeship with George Mitchell, a physician in Elkton, Maryland, and attendance at lectures delivered by Benjamin Rush and other professors at the University of Pennsylvania. Later, after becoming a physician, Evans earned the distinction of being appointed the U.S. Navy's first Surgeon of the Fleet.

The world that Evans and other shipboard surgeons inhabited was a gritty one, beset by administrative tasks. Surgical skills were used in the service of daily complaints, such as infections, food poisoning, occupational traumas such as fractures, dislocations, and hernias, and during outbreaks of contagious disease. Occasionally, these duties were punctuated by frenzied work conducted amid the chaos of battle.

The Marine Practice of Physic and Surgery, a manual of shipboard care published in 1770, described in straightforward terms the standard of care that surgeons should deliver.

"When you are entering on any capital operation, you should use your utmost endeavours to encourage the patient (if he is sensible) by promising him, in the softest terms, to treat him tenderly, and to finish with the utmost expedition; and indeed you should use expedition but not

hurry: you should not make more haste than the care requires, nor cut less than is necessary, or leave any mischief unremedied ... In regard to the wounded, you should act in all respects as if you were entirely unaffected by their groans and complaints; but at the same time ... behave with such caution, as not to proceed rashly or cruelly, and be particularly careful to avoid unnecessary pain."

On Evans's second cruise, the *Constitution* headed for Canada. There, well off the coast of Nova Scotia, it met and engaged in action with HMS *Guerriere*.

During the battle Evans and his mate worked in cramped quarters belowdecks while the din of cannon fire and general mayhem continued overhead. Entry to the area was likely covered with canvas, a drape that was easily removed and washed when it became saturated with blood or bodily wastes. The surgical area's deck was painted red, a color less likely to show blood. During surgical procedures, it was strewn with sand to prevent slipping. Once the operations were completed, the contaminated sand was swept up and flushed overboard.

After the *Guerriere*'s surrender, Evans worked alongside that ship's surgeon to treat the wounded. Later, in his journal, Evans wrote that the wounded prisoners were transferred to the hospital on Rainsford Island in Boston Harbor.

In October, the *Constitution*, with Evans again as surgeon, left port and headed toward Brazil. On December 29, it engaged HMS *Java*. The four-hour battle damaged both ships and took a notable toll on their crews. The *Constitution* lost eight seamen and had another twenty-seven injured. For five of the injured sailors, Evans needed to amputate an arm or a leg.

From 1813 to 1814, Evans was stationed at the Naval Hospital in the Charlestown Navy Yard. It was during this time that he enrolled in HMS and earned his medical degree. ■

Louis Norton, Harvard School of Dental Medicine '62, is a maritime historian and author.







The life of a physician-coroner combines mystery, science, and service by Robert West

THE LAKE CITY of Coeur d'Alene, where I have resided since 1969, lies 30 miles east of Spokane, Washington. The Idaho Panhandle, which is bisected by U.S. 95 and Interstate 90, is surrounded by nearly a million acres of the Idaho Panhandle National Forests. The area is blessed with a multitude of lakes, rivers, and streams. Its lumber mills and mines result in a steady stream of industrial accidents.

Kootenai County has had many physician-coroners. In Idaho, the coroner is an elected partisan position with a four-year term. Since Idaho became a state in 1890, local physicians have acted as coroners in Kootenai County as a part of their civic responsibility. Most coroners in Idaho's forty-four counties, however, are not physicians. In fact, there were only three physician-coroners in Idaho between 1984 and 2010. The Idaho code states only that "The coroner shall be 21 years of age and a resident of the county for one year." Unfortunately, these legal requirements mirror those in many jurisdictions in the United States.

I became a deputy coroner in Kootenai County in July 1970, nine years after graduating from HMS. This happened somewhat surprisingly. William T. Wood, a physician who was then the county coroner, asked me if I would cover coroner calls while he was at a meeting of the Idaho Medical Association. I asked him what my duties would be. He responded: "Raise your right hand."

With a few words, I became a deputy coroner, with the duty and legal responsibility to investigate all deaths by other than natural causes that occurred within the more than one thousand square miles of Kootenai County. With that responsibility came another, one Wood failed to inform me of: "The coroner shall act as sheriff in the event of the death, arrest, or other incapacitation of the sheriff."

I served as deputy coroner, then as the elected coroner, until my retirement in 2011. It was a job that required me to help bring justice to those who died and closure to families that had lost loved ones. It also required me to work collaboratively with law enforcement personnel and other members of my community. It was a challenging job that often brought surprises—and stories.

Toxic Combination

About 1,300 deaths a year are recorded in Kootenai County. Approximately 700 of those fall under the jurisdiction of the coroner. An autopsy—from the Greek word meaning to see with one's own eyes—including toxicology, X-rays, and other tests, costs the county approximately \$2,500. At the time I retired, the pathology and laboratory expense budget was \$160,000 a year. Therefore, we selected carefully cases for which we would order autopsies so as to respect budgetary constraints yet still fulfill our duty to investigate the manner and cause of deaths. The importance of correctly choosing when to conduct an autopsy was often proven to me during my tenure as coroner, poignantly so at times, such as for the case that began on a February night in 1986.

The strobe lights of multiple squad cars were flashing throughout the neighborhood when I arrived. At the mobile command post, I asked the special weapons and tactics team commander to brief me.

"We have a twenty-eight-year-old 'psycho' holed up in this house," the commander said. "He's threatening to kill anyone who tries to enter. The windows and doors are barricaded, the phone lines have been cut, and a shot has been fired. There has been no sign of activity in the house for the past thirty minutes."

The commander continued. "We do not know much else about him. The family reports that in the past few months he became moody, withdrawn, and very paranoid and complained of severe headaches. Kootenai County sheriff deputies have responded to the home several times for domestic violence issues. They say he is an electrician for a local contracting firm."

As we were talking, SWAT team members had surrounded the residence and, receiving no response to their calls to the occupant, had forced the front door open and entered the house. They found the young man dead with a gunshot wound to the head. A revolver lay next to him with a single spent cartridge in the chamber.

After the investigators had completed their systematic investigation of the scene, the on-call funeral home personnel and I entered the home to remove the victim. The detective asked whether there would be an autopsy; it seemed clear the victim had committed suicide. I said that there would be a full autopsy, one that included toxicology, conducted by the Spokane County medical examiner's office.



ON CALL: Ensuring the eviction of a nine-foot python and implicating a control switch for a floating golf green in a man's death are but two of many adventures Robert West encountered during his decades-long tenure as a coroner in Idaho.

Our investigation found that six months before his death, the victim had been working on the electrical system in the mechanical room for the signature floating fourteenth green at the Coeur d'Alene Resort's golf course. The mechanical room contains a system that uses mercury switches to activate pumps that level the green by moving water into and out of ballast tanks. On the day the victim was working in the room, one of those switches exploded, vaporizing the mercury.

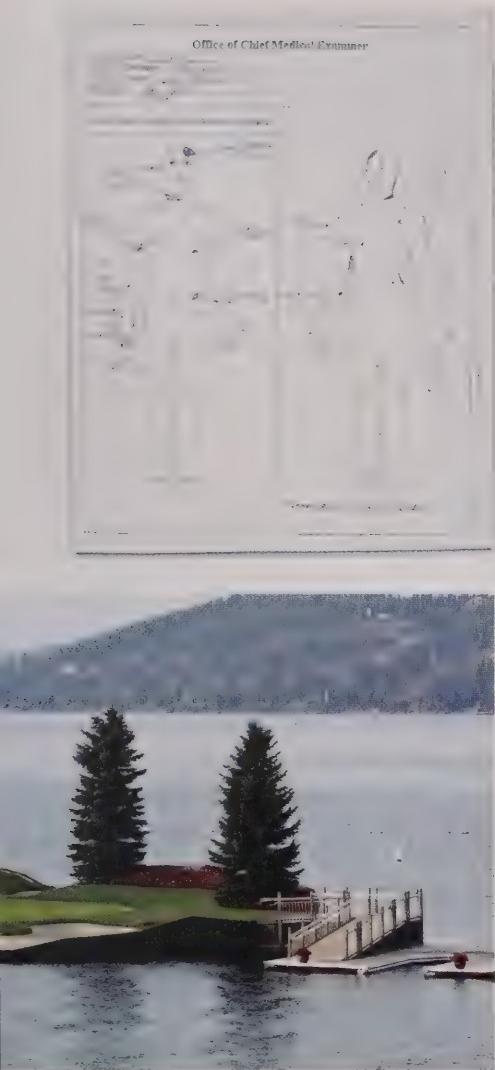
The victim had inhaled toxic mercuric oxide fumes. Although the room had been ventilated and cleared of the poisonous fumes, the electrician had not been evaluated by a physician.

The toxicology report indicated a marked elevation in the victim's serum mercury levels. Further testing showed that chronic mercury poisoning was the likely cause of the deterioration of his mental status.

The victim had suffered from Mad Hatter's syndrome. Long before Lewis Carroll penned *Alice's Adventures in Wonderland*, hatmakers

used mercury compounds while working felt for hats. The exposure to mercury had caused many to experience headaches, anemia, personality changes, and dementia.

The electrician's death was the result of an industrial accident, not a suicide. The subsequent wrongful death lawsuit filed by the victim's family did not make me any friends among the resort's management. It did, however, help explain why the young man died as he did. It also illustrates the type of investigation that can be necessary, even in rural Idaho; coroners and medical examiners need to make their own investigation in each case and to assess information gathered from both the autopsy and toxicology analyses.



Takeout Order

I grew up in rattlesnake country in North Dakota. At a young age, I learned never to put my foot down without first looking for a snake.

I fully appreciate the value of snakes in controlling vermin such as rats and mice. Nevertheless, I have a certain visceral reaction to reptiles that I've never lost. For me, one of North Idaho's main attractions is its absence of poisonous snakes. Unfortunately, what doesn't exist in the wild does exist in some homes.

In 2010, a reclusive man in Rathdrum, Idaho, called the police asking for medical assistance. A convicted felon, he had moved to Rathdrum after his release from prison. Aside from some calls espousing his radical ideas about society or complaining about people trespassing on his property, the police had had little contact with him. He had severe chronic obstructive pulmonary disease and was under the care of the VA Hospital in Spokane.

When he called, he said he would meet the officer and paramedics on his front porch. They were not to enter his house. The

ambulance arrived and took him to Kootenai Medical Center in Coeur d'Alene where, unfortunately, he died. His estranged family lived in Pittsburgh. They asked that his household items be shipped to them.

When the officers went to pack up the man's belongings, they found a menagerie of exotic animals, including several pythons, an iguana, and several large scorpions, as well as a supporting cast of rats, mice, and rabbits representing the reptiles' menu.

One of the Rathdrum police officers had an aversion to snakes akin to mine. He contacted Panhandle Pet Rescue, an organization primarily involved with stray cats and dogs. The woman there knew of the man and his exotic pet collection. She captured and took several of the snakes, the iguana, the scorpions, and the other animals to the rescue facility. As she left, she told officers: "I couldn't find the nine-foot python I gave him about three months ago." It turns out, neither could the officers.

My chief deputy coroner related this story to me when I returned from a forensic medicine seminar. I called the Rathdrum police and talked to the officer who had first responded to the call. He was not interested in making another trip to that house. He said, "Doc, I really do not like snakes!" I said, "What if there is a python in that house and some stranger or kid gets in there when the python is really hungry? Do me a favor, have the Panhandle Pet Rescue lady go through the house with you one more time."

He reluctantly agreed to do so. About two hours later, I got the call—"Okay, Doc, there was a nine-foot-long Burmese python behind a desk in the living room." Panhandle Rescue removed the reptile, and both the police officer and I slept better that night.

Truth Be Told

It has been reported that in the United States, only 12 percent of physicians responsible for completing and signing death certificates have training in correctly listing the cause and manner of death. The error rate on these certificates approaches 30 percent. In addition, many who fill out death certificates are reluctant to list socially unacceptable causes or manner of death (such as syphilis, alcoholism, alcoholic cirrhosis, HIV/AIDS, suicide, or homicide).

In my experience, the vast majority of coroners and medical examiners are extremely professional and diligent in performing their duties. They operate with scant resources in remote communities and

face the scrutiny of the public, law enforcement, and the justice system. They must exhibit professional standards equivalent to those of the most advanced forensic medical examiner's office and must maintain smooth working relationships with law enforcement, funeral homes, the public, and the media.

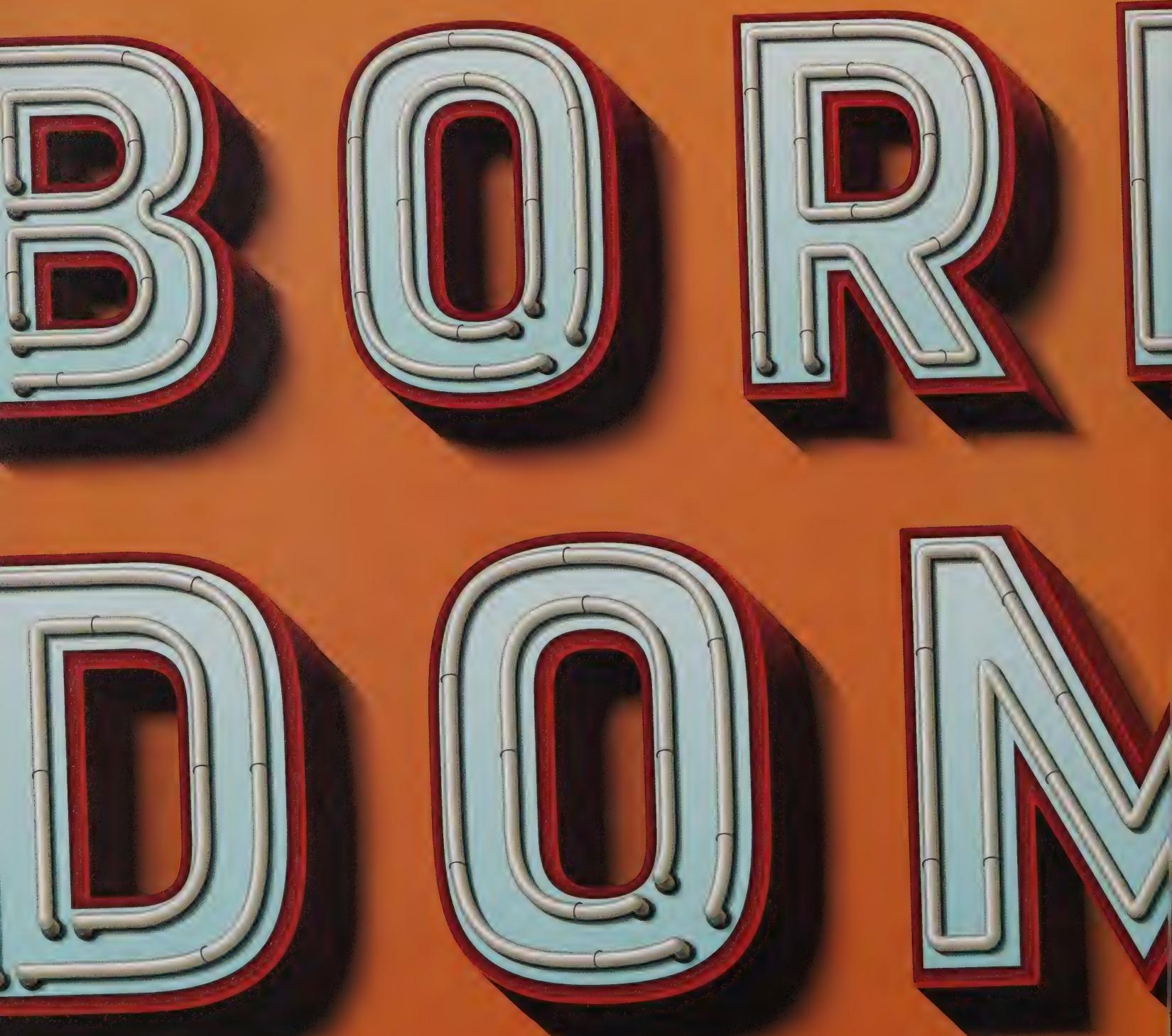
The coroner/medical examiner position is a 24/7, 365-days-a-year job. You cannot do it from behind a desk. You must be willing to be the boots on the ground, even if it means rolling out of bed at midnight and driving 30 miles over logging roads clogged with snow to investigate an accident scene. You have to do your own investigation from the unique viewpoint of the coroner. Of course, you will get a briefing from the on-scene law enforcement officers. Family members provide valuable information about the deceased, as do other witnesses. But ultimately, the coroner is the ombudsman for the deceased.

Nationally, there is a dichotomy between the public's perception and the realities of the coroner/medical examiner system. The public assumes all coroners are board-certified medical examiners with the training, facilities, and expertise to produce uniformly accurate results in one hour or less, as seen on television's *CSI*. The 2011 *Frontline* public television documentary *Post Mortem* chronicled a dismal picture of some of the worst deficiencies of the current coroner/medical examiner system. State and local funding entities do not come close to supporting the type of forensic systems necessary to provide even basic functions. Many coroners are not prepared to personally investigate cases on the scene, regardless of the circumstances, distance, or time of day.

There are few incentives to attract physicians or other professionals to the field. Medical students and pathology residents are seldom encouraged to enter this field of medicine. The financial rewards pale in comparison to those for most other specialties. But my hope is that my experiences as coroner in Kootenai County might be used to encourage medical students to consider the field of forensic medicine and to begin a discussion about improving this country's coroner/medical examiner system. The public needs—and deserves—a better system. ■

*Robert West '61 lives in Coeur d'Alene, Idaho. This story is adapted from his book, *It Can (and Does) Happen Here!* One physician's four decades-long journey as coroner in rural north Idaho, published in 2014 by Abbott Press.*

Could it be creativity's spark—or a cause for concern? by Perri Klass

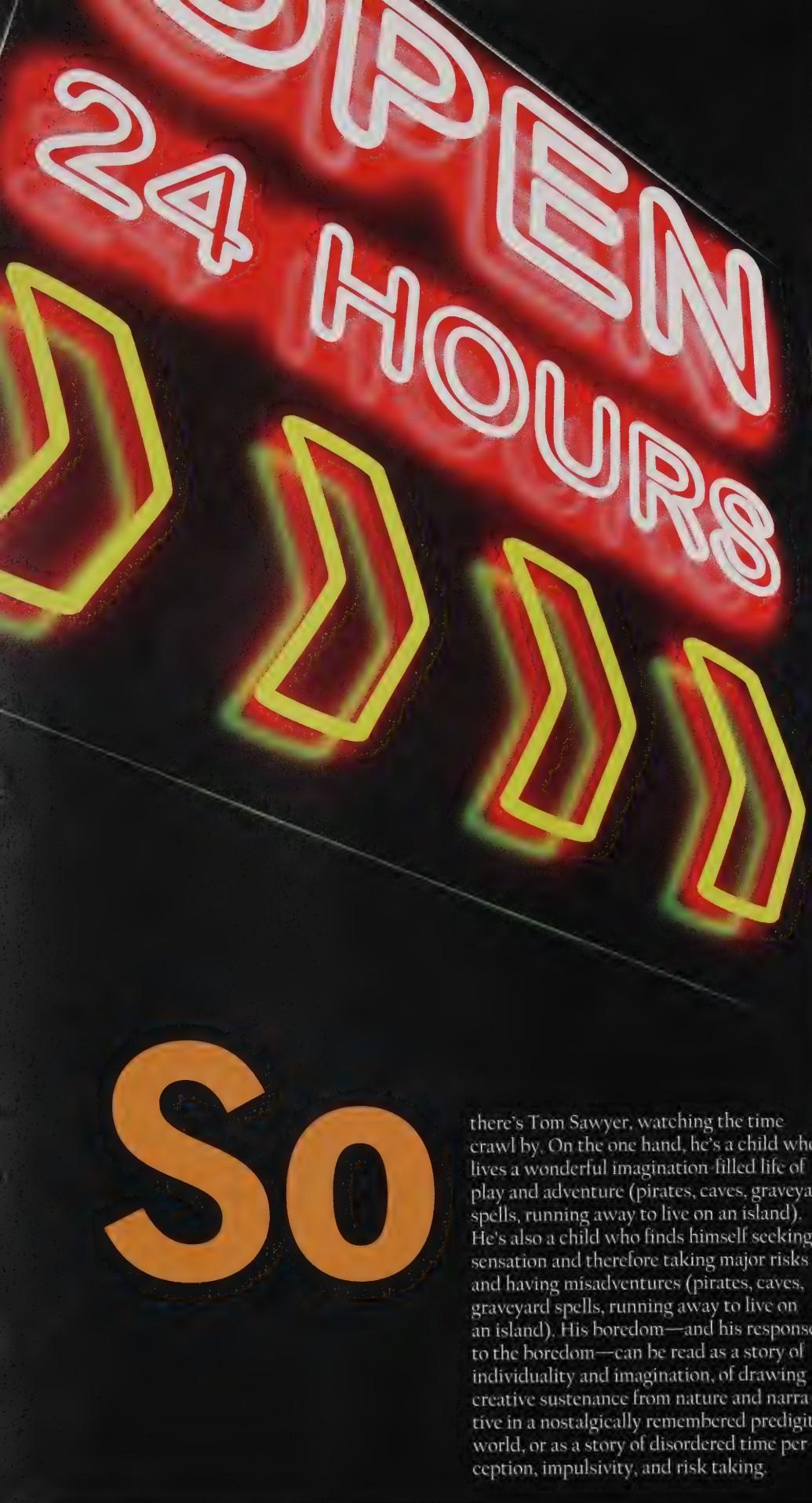




From *The Adventures of Tom Sawyer* Monday morning found Tom Sawyer miserable. Monday morning always found him so—because it began another week's slow suffering in school. He generally began that day with wishing he had had no intervening holiday, it made the going into captivity and fetters again so much more odious.... The harder Tom tried to fasten his mind on his book, the more his ideas wandered. So at last, with a sigh and a yawn, he gave it up. It seemed to him that the noon recess would never come. The air was utterly dead. There was not a breath stirring. It was the sleepiest of sleepy days. The drowsing murmur of the five and twenty studying scholars soothed the soul like the spell that is in the murmur of bees. Away off in the flaming sunshine, Cardiff Hill lifted its soft green sides through a shimmering veil of heat, tinted with the purple of distance; a few birds floated on lazy wing high in the air; no other living thing was visible but some cows, and they were asleep. Tom's heart ached to be free, or else to have something of interest to do to pass the dreary time. »

MATTIAS PALUDI





there's Tom Sawyer, watching the time crawl by. On the one hand, he's a child who lives a wonderful imagination-filled life of play and adventure (pirates, caves, graveyard spells, running away to live on an island). He's also a child who finds himself seeking sensation and therefore taking major risks and having misadventures (pirates, caves, graveyard spells, running away to live on an island). His boredom—and his response to the boredom—can be read as a story of individuality and imagination, of drawing creative sustenance from nature and narrative in a nostalgically remembered predigital world, or as a story of disordered time perception, impulsivity, and risk taking.

Boredom—at least in children—may be having something of a moment, with parenting experts, psychologists, educators, and even neuroscientists expressing public concern that children today lack true down time. Some see the modern child as overscheduled by ambitious parents, shuttled from high-pressure sports practice to tutoring to cultural enrichment activities. Others lament that the easy availability of electronic devices means never having to spend a single moment bereft of the opportunity to play a game, or text a friend, or watch a video.

If you're looking for medical models for boredom, you could think of it as a kind of angina, the pain of temporary oxygen deprivation, that causes a tissue to protest that it is starved for an essential nutrient. We are designed to be interested, and boredom may be the brain's way of telling us something is missing.

Daydream Believers

Yet if a child doesn't get to spend some time in that problematic state, how will that child ever learn to find the way out?

"I am concerned about the fact that we stimulate our kids and ourselves twenty-four/seven as if boredom or emptiness were toxic things," says Michael Rich '91, an HMS associate professor of pediatrics and director of the Center on Media and Child Health at Boston Children's Hospital. "Boredom can be a very good thing; that's when kids say 'let's build a treehouse, let's put on a puppet show.'"

Rich suggests that the danger of an overstimulated childhood is that children may never learn to find the imaginative paths that lead them out of that unhappy bored state. "Parents can teach kids and model for kids that it's okay to not have an agenda, to not have something to do, to just walk in silence in the woods, to just lie on your back in the grass and make shapes out of clouds," he says, so that "not only do they learn to tolerate that so-called emptiness but they learn to enjoy it. That's where creativity and innovation come from."

Teresa Belton, an educational researcher at the University of East Anglia in the United Kingdom, has spoken about the link between boredom and creativity, arguing that too much exposure to screens stunts the development of imagination and inner resources. She and a colleague interviewed successful people, including a novelist, a poet, an artist, and a neuroscientist, for a

project on creativity and found that all cited boredom as an important—and helpful—source of creative endeavor and inspiration.

The neuroscientist in the study was Baroness Susan Greenfield, an Oxford professor, who has also spoken widely on the benefits of boredom and the pitfalls of too-readily available entertainment. She notes that in our modern society, we have overscheduled our children with programmed activities and handed them many forms of entertainment that essentially provide them with narratives, rather than leaving them to invent their own.

"In the past, boredom was a good thing because it provided an impetus for you to develop your narrative," she says. "A tree in the park didn't ask you to climb it, a drawing pad didn't ask you to draw on it—you weren't bored because you made up a story."

Here We Are Now, Entertain Us

A couple of decades ago, when I was relatively new to practicing pediatrics, a nine-year-old boy came to see me for a physical. His mother brought along a note from his teacher, asking to have the child evaluated for attention-deficit disorder. The note indicated that he simply could not pay attention in class. I asked my patient directly: did he feel it was hard to concentrate in school? He said, "She's a boring teacher. I already know all this stuff." Then he dug into his backpack and produced sheaves of worksheets, endless fill-in sentences, all correctly completed. "It's all too easy," he said. "I'm bored all the time."

"There's a differential diagnosis for 'I'm bored in school,'" says Barbara Howard, a developmental-behavioral pediatrician at Johns Hopkins School of Medicine, "and one possibility is, it's boring in school, you may have a boring setting. But the more likely thing when they come to me is they're gifted, or they have ADHD, or both."

Boredom in school-age children, in school or out, raises a range of issues on both ends of the classroom achievement spectrum. According to Howard, among developmental behavioral pediatricians, boredom is a common distinguishing marker for ADHD. In fact, it has been suggested that Tom Sawyer would nowadays carry that diagnosis. A child with learning issues, way out of depth in math or reading, may also report being bored, as might the best math student in the class. So might a child who is having trouble concentrating because of anxiety about problems at home.

Some of us think of ourselves as easily bored; others are fiercely proud of never being bored, which should probably in itself be regarded as a danger sign of something.

When children complain of boredom outside a specific classroom context, they may actually be expressing a different, deeper need. "When children or teens say they're bored, I always think they're searching for what they actually feel," says Michael Thompson, a clinical psychologist, supervising psychologist at Belmont Hill School in Massachusetts, and the author of several books, including *Raising Cain: Protecting the Emotional Life of Boys*.

"Imagine you have a child saying, 'Mom, I'm bored,'" he says. "It means a child may be saying, 'Mom, I want more attention from you and I don't know how to ask for it, and I may not even know that I want more attention. I'll just come up to you and say 'I'm bored,' so you'll do something.'"

A nine- or ten-year-old who wishes he had more friends or a different group of friends may say he's bored, as might an adolescent who is deeply bothered by complex feelings he can't quite explain. Adds Thompson, "A fifteen-year-old might say, 'Mom, I'm bored,' and mean 'I'm angry that I have no control over my life; I'm hating the existential condition of being fifteen, and I know there's nothing I can do about it or that you can do about it,' but the comment will start a little fight, and then there'll be some action."

That transition from boredom to action—an action, including conflict—is what

makes the chronically bored child the object of psychological and educational concern. So while psychologists and educators speculate about the beneficial effects of a little boredom in the life of the modern child, they also warn that too much boredom is associated with problems ranging from school failure to dropping out to juvenile delinquency to alcohol abuse and gambling.

In an article published in 2012, John Eastwood, an associate professor of psychology at York University in Toronto, and his colleagues proposed a definition of boredom: "the aversive experience of wanting, but being unable, to engage in satisfying activity." The key components, they said, were a desire to engage, coupled with a failure to engage, and an awareness of that failure. "It involves this intense desire to connect with the world," says Eastwood. The intensity of that desire can also bring the risk of connecting with the world in negative ways, including aggression.

The Eastwood article also argues for a component of awareness—to be bored, you have to know that you're bored. Some of us think of ourselves as easily bored; others are fiercely proud of never being bored, which should probably in itself be regarded as a danger sign of something.

Peace of Mind

Which brain is bored: the whirring overactive brain, too conditioned to electronic gratification, or the sluggish depressed brain, refusing to find value or interest in a world full of complex beauty? Should we celebrate the child who complains of boredom and that long rich history of childhood tedium? And should we congratulate the parents and the teachers who foster the development of a rich inner life by not rushing in with entertainment and organized activities? Or should we worry that the child who complains of boredom is sending an important distress signal, heralding school failure, social marginalization, and dangerous risk-taking behaviors?

"Boredom is a normal part of human existence," notes Eastwood, adding that he wouldn't want to see it become another form of psychopathology.

"But," he continues, "it should be taken seriously." ■

Perri Klass '86 is a professor of journalism and pediatrics and director of the Arthur L. Carter Journalism Institute at New York University.





A Common

VECTOR ANALYSIS:
Bats, such as these
fruit bats, can harbor
the Ebola virus and
may have been the
zoonotic origin of the
recent epidemic in
West Africa.

STEPHEN R. CHEP MENDENHALL / MENDENHALL PHOTOGRAPHY

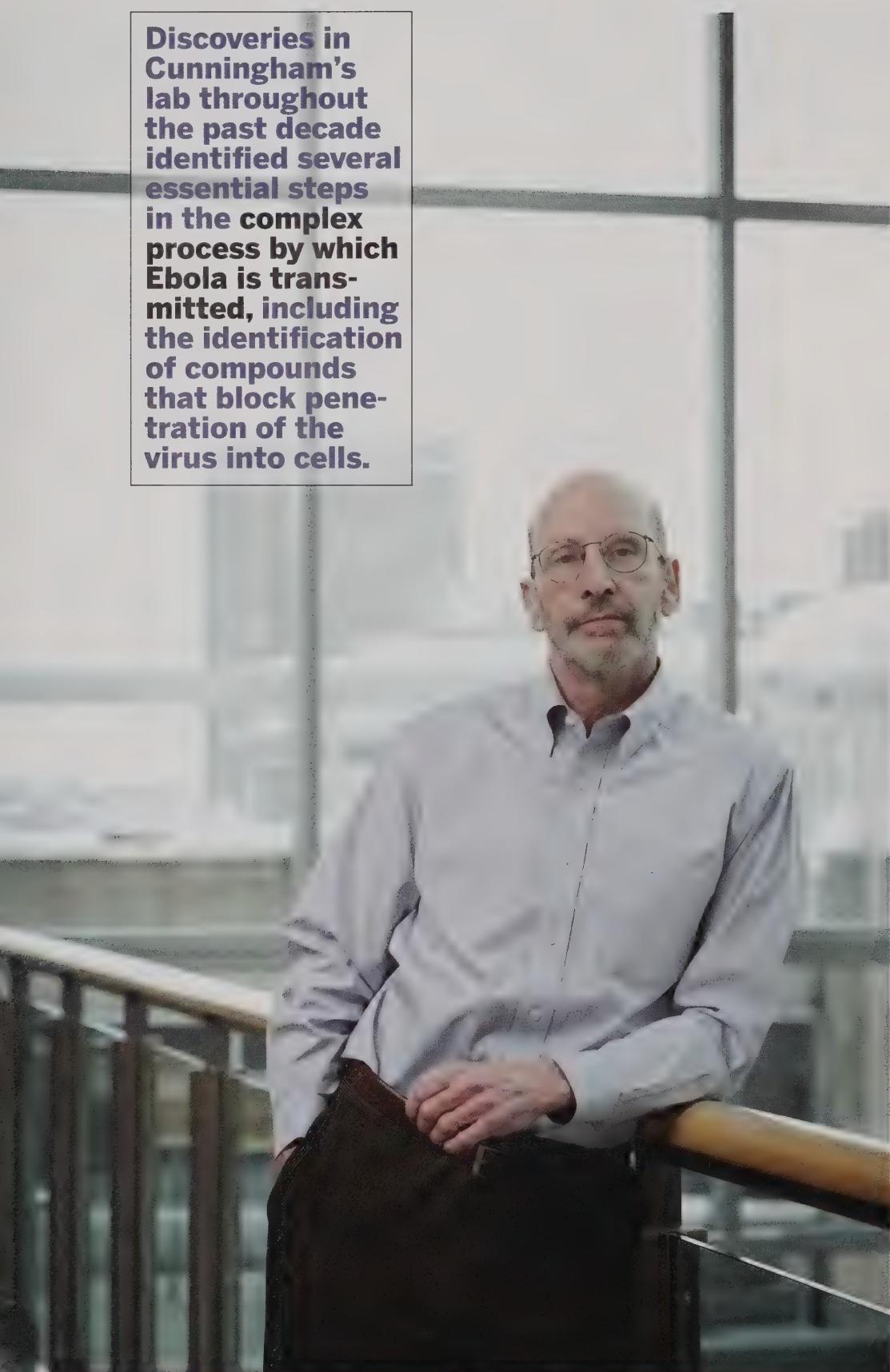
Foe

Members of the HMS
community brought myriad skills
to the fight against Ebola
by Debra Bradley Ruder

Last fall, as Ebola, a highly contagious and deadly hemorrhagic illness, tore through West Africa, devastating families and straining fragile health systems, infectious disease physician Megan Murray '90 jumped into action. Like others at HMS, Murray, an HMS professor of global health and social medicine, director of the research core in the HMS Department of Global Health and Social Medicine, epidemiologist, and world-recognized expert in tuberculosis, began identifying urgent research questions raised by the epidemic and turned to HMS colleagues to help answer them.

"We involved a lot of individuals who were working extraordinarily hard," Murray says.

Discoveries in Cunningham's lab throughout the past decade identified several essential steps in the complex process by which Ebola is transmitted, including the identification of compounds that block penetration of the virus into cells.



Throughout the HMS community, clinicians, bench scientists, data specialists, global health and humanitarian crisis experts, and others brought their knowledge to bear on the largest Ebola epidemic in history.

Discovered in 1976 near the Ebola River in Central Africa, the virulent virus was a rarity in West Africa. Yet, in December 2013, an unidentified virus killed a toddler in Guinea. The infectious agent spread quietly into neighboring Liberia and Sierra Leone and then erupted, spreading rapidly within the three countries, aided by poor communication, limited medical infrastructures, social forces, and a tentative international response. By late February 2015, the disease had been verified as Ebola. By mid March, the virus had sickened an estimated 24,700 people and killed more than 10,000 in West Africa. Since that dire high point, the number of new infections has been steadily falling, and responders are working toward the magic number of cases: zero.

Although the epidemic's intensity has diminished, the work of HMS researchers in Boston and Africa has not. Scientists and clinicians such as those profiled here are continuing their efforts to contain the disease and to prevent future outbreaks through better diagnosis, treatment, health systems, and access to quality medical care.

Portals Being Stormed

Long before the Ebola virus became daily news, James Cunningham, an HMS associate professor of medicine (microbiology and molecular genetics) at Brigham and Women's Hospital, had been studying how enveloped viruses like Ebola enter cells and wreak havoc. Discoveries in Cunningham's lab throughout the past decade identified several essential steps in the complex process by which the Ebola virus is transmitted, including the identification of compounds that block penetration of the virus into cells.

Although these findings have contributed to our overall understanding of the Ebola viruses, it was only recently—as the epidemic in West Africa intensified interest in finding effective therapies and vaccines—that Cunningham's work took a significant step toward drug development. In January, Harvard University and Brigham and Women's licensed two classes of Ebola inhibitors to a biotechnology company in Canada for development.

One class targets a host protein, Niemann-Pick C1, which normally trans-

ports cholesterol into cells. Cunningham and his colleagues found that Niemann-Pick C1 is an essential part of the portal that Ebola uses to enter cells.

"If Niemann-Pick C1 is absent or blocked, infection doesn't occur," says Cunningham. "That gives us confidence that it is a good drug target."

A second family of compounds disrupts Ebola's path to the lysosome, the cell compartment containing Niemann-Pick C1; a major goal is to understand how this second family of compounds works.

Cunningham's team described the critical role of Niemann-Pick C1 in Ebola infection in a 2011 paper in *Nature*. That report built on the team's earlier research showing that specific proteases in the lysosome help Ebola enter cells. Their findings coincided with those in a separate *Nature* study published by colleague Sean Whelan, an HMS professor of microbiology and immunobiology, whose lab used a genetic approach (rather than Cunningham's chemical biology one) to identify the proteins required for infection. The studies refined our understanding of Ebola by revealing why sequential encounters with host protease and Niemann-Pick C1 are essential for infection.

Cunningham hopes that the compound that targets Niemann-Pick C1 can be developed into a low-cost and easily produced oral treatment for Ebola, especially given the absence of proven therapies beyond supportive care with IV fluids. There are currently no antiviral medicines or vaccines approved by the U.S. Food and Drug Administration for Ebola, although several are being tested.

"Producing an effective new therapy for Ebola would be incredibly gratifying for my colleagues and me," says Cunningham. "That possibility provides an additional strong incentive to continue our studies."

Safety First

Michelle Nescierenko, an HMS instructor in pediatrics and director of the Global Health Program at Boston Children's Hospital, usually spends four or five months a year in Liberia as part of an academic consortium, which is led by the University of Massachusetts Medical School and includes Boston Children's, that works to strengthen medical education. She was in Liberia in June 2014 teaching advanced life support to medical residents when the Ebola virus was diagnosed in residents of a crowded neighborhood in Monrovia, the capital city. An



STANDING ORDER: Ensuring government hospitals in Liberia are well supplied with infection-control gear is part of an intervention system designed by Michelle Nescierenko and colleagues.

earlier outbreak in the country was thought to have been contained months before, so the news of new infections made her heart sink. Liberian health care workers already faced routine shortages of gloves, gowns, and other infection-control essentials, and "we knew the system was never going to be able to cope with the need for Ebola protection," says Nescierenko. The disease spreads in humans through contact with infected bodily fluids and causes fever, severe headache, bleeding, vomiting, diarrhea, and, often, death.

During this past summer while Nescierenko was in Boston, Ebola continued to spread through West Africa. Health care facilities, overwhelmed by the volume of patients and the risk of Ebola infection, closed. Individuals with conditions other than Ebola were afraid to seek care, and hundreds of providers—including several of Nescierenko's Liberian friends and coworkers—contracted the virus. "When we returned in November, it was like the sky was still falling," Nescierenko recalls.

She dove in, coordinating a relief effort through the consortium to restore basic

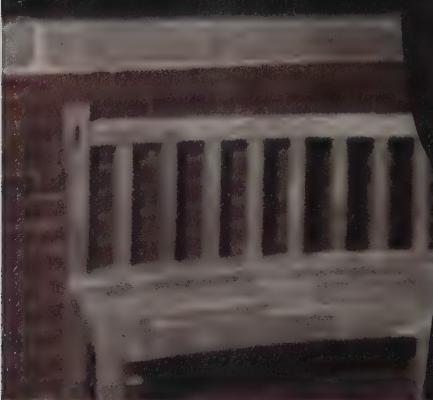
health care by reopening hospitals and training and protecting frontline staff. "We've focused on keeping Ebola out of hospitals and on teaching providers how to practice safely," she says. An intervention she co-designed sends teams of Liberian trainers, including doctors, nurses, midwives, and water and sanitation engineers, to twenty-two government hospitals across the country, and the team coaches hospital staff on proper triage and other safe practice standards. Each hospital receives a three-month stock of personal protective equipment (PPE) and other infection-control gear as well as follow-up visits or check-in calls.

In January, Nescierenko saw encouraging results at Redemption Hospital in Monrovia; there, the contagiousness of Ebola had made caregivers wary of touching patients. As she was walking by the pediatric ward, she looked through the window and saw two nurses "wearing proper PPE—gowns, gloves, and shields to protect their faces—and they were putting an IV line into a very sick baby who, probably, nobody would have touched two weeks earlier," she says. "So the training makes a difference. It's ultimately going to help make their system stronger."

The Crisis at Home

For the past eight years, Last Mile Health, a nonprofit led by Rajesh Panjabi, an HMS instructor in medicine and associate physi-

Last Mile Health, the nonprofit led by Panjabi, has trained 340 health facility staff and more than 900 community health workers in identifying and tracking Ebola.



cian in the Division of Global Health Equity at Brigham and Women's, has been working in Liberia, delivering primary care to remote rainforest villages. Last Mile Health trains and equips community health workers to treat malaria, pneumonia, complications of childbirth, and other high-mortality conditions within their local communities.

A Liberian native, Panjabi co-founded the organization in 2007 to serve those his family had left behind when they escaped that nation's civil war in 1990, when he was nine years old. "After the conflict, the country had fifty-one physicians for about four million people," says Panjabi.

The organization's mission gained urgency after Liberia announced its first suspected Ebola cases in March 2014; by July, the group was coordinating response efforts in partnership with the Liberian government. To illustrate Ebola's destructive nature, Panjabi relates the story of one woman in Rivercess County, one of two counties where Last Mile Health works. "She was infected with Ebola when she left Monrovia in late October. She traveled ten to fifteen hours into the rainforest in Rivercess, then fell ill. The community didn't have the resources to bury her safely.

Fourteen days later, fourteen people had died of Ebola, forty people were infected, and ninety were exposed. All this happened way in the heart of the rainforest."

For its part, the organization has trained 340 health facility staff and more than 900 community health workers and other villagers in identifying and tracking Ebola—including going door-to-door to identify sick people, get them treatment, and trace their contacts to prevent further contamination. Last Mile Health also has continued dispensing malaria tablets, antibiotics, prenatal care, and other essential services through its network of local health workers.

The government of Liberia plans to dramatically expand the country's health workforce, including scaling up efforts like Last Mile Health's community-based model, according to Panjabi. "If that happens, we'll have a health worker in every village in every part of the country. That's the kind of thing that stops threats like Ebola from becoming threats to everyone everywhere."

Ground Control

Do some people who harbor Ebola virus stay healthy? What's the lag time between

showing symptoms and being infectious? Will survivors face long-term physical and social consequences?

According to Murray, answering these questions will help elucidate how Ebola tightens its grip on individuals and populations and, researchers hope, lead to better treatment outcomes and containment practices. The work complements that of others in the School's Department of Global Health and Social Medicine, including the on-the-ground clinical activities of Paul Farmer '88, the Kolokotrones University Professor of Global Health and Social Medicine, and Partners In Health, the organization Farmer co-founded.

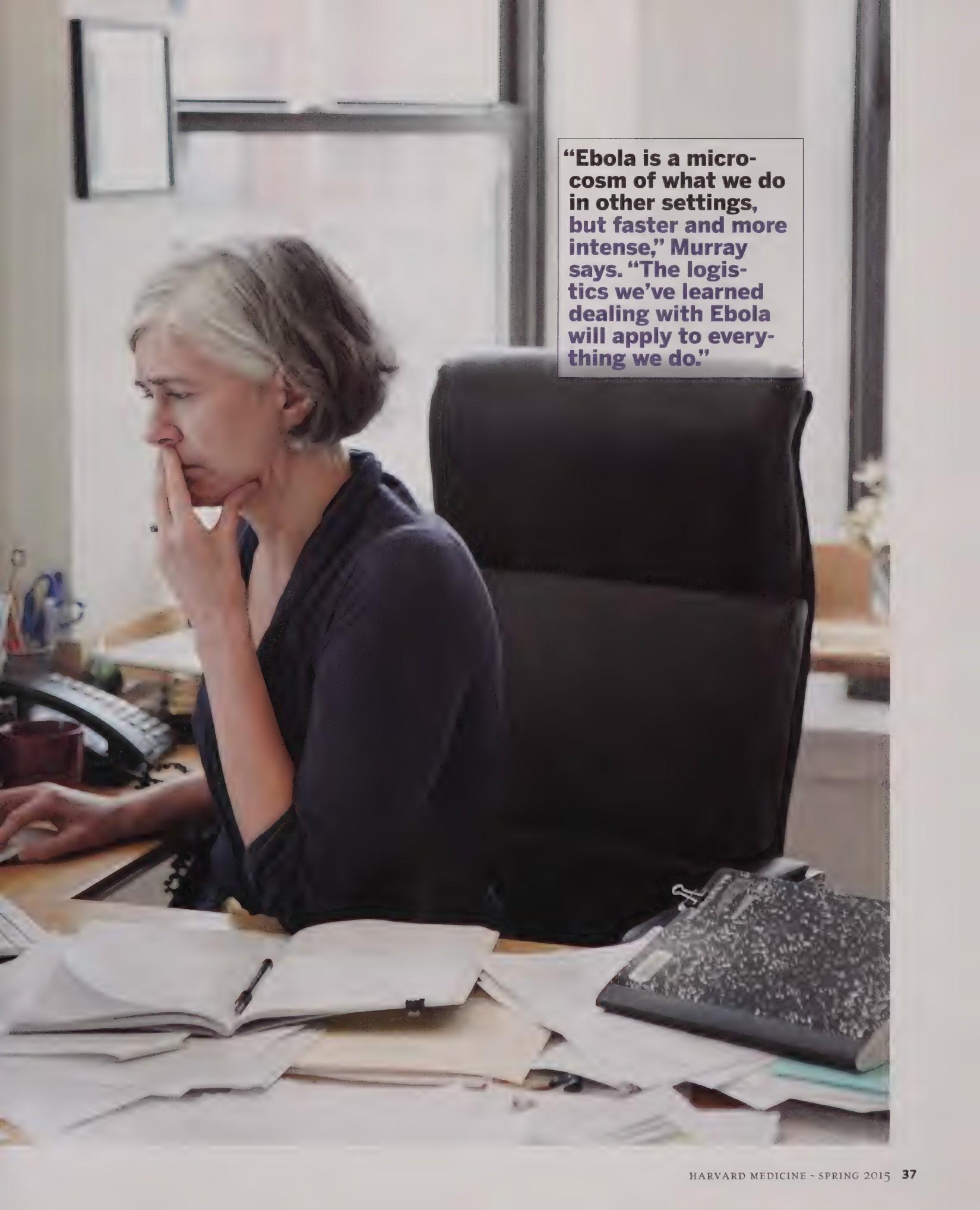
Capturing meaningful patient data is particularly challenging in the chaotic environment of a West Africa Ebola clinic, she adds, where patients are gravely sick; lab capacity, electricity, and Internet service are limited; caregivers must wear hot and cumbersome protective gear; and even paper with clinical notes has to be destroyed because it is contaminated.

In a related effort, Eric Perakslis, executive director of the HMS Center for Biomedical Informatics, has collaborated with Médecins Sans Frontières and Google Crisis Response on a clinical data management tool that allows providers in highly infectious or toxic environments to document patient encounters accurately, safely, and quickly. "It's a complete electronic health record in a box," says Perakslis. This winter, he spent two weeks in Sierra Leone piloting the system, which runs on Android tablets.

Murray's team also has several Ebola-related clinical studies under way. One, which launched in February and involves Nira Pollock, an HMS assistant professor of medicine at Beth Israel Deaconess Medical Center, will examine the accuracy of point-of-care diagnostic tests that provide immediate results, a major advantage in a region with scarce laboratory services. A second project will track the experience of Ebola survivors for eighteen months after treatment, exploring such factors as immune response, health problems, and social integration.

The Ebola epidemic in West Africa waned faster than expected, so one lesson going forward, says Murray, is to activate data collection systems as quickly as possible. "Ebola is a microcosm of what we do in other settings, but faster and more intense," she says. "The logistics we've learned dealing with Ebola will apply to everything we do." ■

Debra Bradley Ruder is a Massachusetts-based education and health care writer.



"Ebola is a microcosm of what we do in other settings, but faster and more intense," Murray says. "The logistics we've learned dealing with Ebola will apply to everything we do."





The Burden of Proof

Kids helping kids helping science—that's the promise of pediatric clinical trials **by Elizabeth Cooney**

Four doctors file into Becca's hospital room on their daily rounds, thirteen days after the teenager received a stem cell transplant. They rub their hands with sanitizing gel, then proceed to listen to her chest. The stethoscope they use stays in her room; when not in use, it hangs from the IV pole. An array of hair bows pinned next to cheerleading pictures on one wall leads a doctor to venture that Becca's room could win a best-decorated contest.

The 15-year-old says she always wears a bow in her hair. Not losing her hair to chemotherapy is perhaps the most tangible sign of the gentler approach doctors are taking to treat her rare disease. Dyskeratosis congenita is an inherited disorder in which telomeres—the protective caps on the ends of chromosomes—are not properly maintained, a situation that can lead to changes in the controls on cell division. Becca's rapidly dividing cells burn out quickly, leading to bone marrow failure. Because her cells do not repair damage as well as they should, she is more susceptible to cancer and organ failure.

The chemotherapy or radiation typically used to prepare a body for a bone marrow transplant is extraordinarily harsh, and Becca's condition makes her even more vulnerable to the aggressive nature of these conventional tools. To help her body accept the donated stem cells, doctors instead gave Becca immunosuppressive drugs only. In other studies, this approach has shown that

the more robust cells will outcompete the leftover damaged cells and will survive.

One of Becca's doctors wears two hats: clinician and researcher. He oversees her care—and the research study's protocol. Becca is one of five participants in the pilot study.

Her parents wouldn't have it any other way. Their unease with having their daughter be one of only a handful of patients in the world to receive this alternative treatment was calmed when they learned that their daughter's doctor is an expert in her disease. Today, the disease neither of them had heard of until Becca's diagnosis four months ago has become their own object of study. They know her dates and diagnoses; they understand there is a 10 percent risk that her body won't accept the transplanted cells or be able to produce its own. They check her online patient portal daily to see what her blood counts are, willing her absolute neutrophil count above 500, the threshold of transplant success.



"You just watch the numbers and pray," her mother says. "There's nothing else you can do. Whether you believe in God or not, you pray."

Small Trials

Clinical trials like Becca's propel progress in medicine, especially in children's cancer, oncologists and scientists say. Yet by definition, research is a search for answers. Scientists, clinicians, ethicists, parents—and sometimes children—must make decisions that balance potential risk against potential benefit for one child, and, ultimately, for all children.

Testing new therapies in children has become more common since the 1960s. Then, a drug protocol was a math problem in which an adult dose was divided by a child's weight. Although more is now known about how drugs affect children at different developmental stages, most drugs used today in children have never been tested in children.

"For eons, cultures treated children as small adults. The same can be said for medicine," says Alan Guttmacher '81, director of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. "Yet, it's clear they are not small adults, and in terms of therapies that fact has specific impact."

Children, for example, don't metabolize drugs the same way adults do. Toxicities vary for young, developing organs; what is toxic to a 6-month-old may be differently tolerated by a 6-year-old, and tolerance may again change for a 16-year-old. Each may show a significantly different degree of toxicity when compared with that of a 60-year-old. In addition, because of individual genetic and



physiological differences, there will likely be internal variation within any age group.

In the Balance

Fears over harming vulnerable children in the name of research, however, may have produced unintended consequences.

"We protected children so long from research experiments," says Susan Kornetsky, director of clinical research compliance at Boston Children's Hospital, "that each time we prescribed a drug for them for which there was no pediatric data, we actually subjected children to an uncontrolled experiment. You had to select a drug tested only in adults, and then take your best guess that maybe it would work the same way in children." As a member of her hospital's institutional review board (IRB), Kornetsky is responsible for reviewing research protocols to ensure they meet regulatory and ethical standards.

The enrollment of children in research studies has risen throughout the past decade. Among children under the age of 15 who are diagnosed with cancer, roughly six out of every ten participate in clinical trials. This rather robust enrollment rate may be attributed to the fact that the relative rarity of cancer in children means that the 15,000 children diagnosed with the disease annually in the United States will more likely be cared for at academic medical centers, focal points for clinical research. Among adults diagnosed with cancer, fewer than one in twenty participate in clinical trials.

IRB panels must weigh the likelihood that a child will be put in jeopardy or reap a benefit by participating in a research trial. If no other

treatment will work, the balance tilts toward benefit. If, however, other treatments are available, federal regulations say the anticipated risk and benefit to the child in the trial must be equivalent to those from alternative approaches. That standard does not exist for adults.

"That's where the regulations and ethics get a bit fuzzy," says Robert Truog, director of the HMS Center for Bioethics and the HMS Frances Glessner Lee Professor of Medical Ethics, Anaesthesia, and Pediatrics at Boston Children's. "If a child can benefit from the research, then that's a justification for exposing that child to more than minimal risk in a research study. But if you have good reason to believe that the treatment is beneficial, then you should be using it as a treatment and not limiting its use through clinical trial. By definition, when you're doing clinical research, you don't know whether what you are about to do is going to be beneficial or harmful."

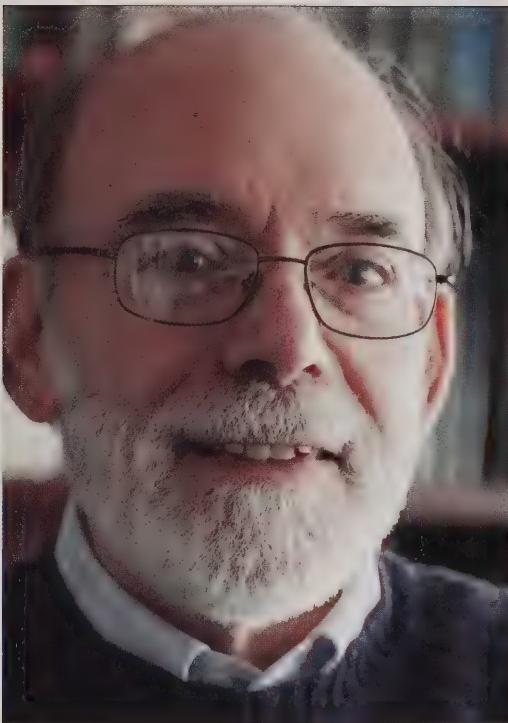
Kindness of Strangers

Doctors who double as researchers are careful to guard against confusing the mission of providing the best care with that of furthering the science. They take pains to explain to potential study participants what is known and what they hope to learn, all to avoid any "therapeutic misconception" that might arise in the minds of patients or in those of parents who are weighing whether to enroll their child in a research trial.

Paul Appelbaum '76, director of the Division of Law, Ethics, and Psychiatry at Columbia University, coined the term therapeutic misconception some thirty years ago. He says parents may be particularly prone.



CONSIDER THE CHILDREN: Making sure young patients, and their parents, understand the principles of clinical trials is central to the work of Robert Truog (far left); Mark Kieran, Amy Billett, and Leslie Lehrmann; Alan Guttmacher; Paul Appelbaum; and Susan Kornetsky.



"Many research subjects hold on to the idea that the doctor will decide what's best for them," Appelbaum says. "When consenting on behalf of their children, parents may be particularly likely to focus on the possible benefit and to ignore the fact that the study is not intended solely to benefit their children."

Clinicians can help undercut misconceptions by explaining the differences between treatment and research, including the role of placebos, which are inactive medications administered as checks on the efficacy of the medication being studied, and by explaining that, unlike in clinical care, research protocols may restrict the degree to which drug dosages may be adjusted.

Kornetsky urges families to talk with their family doctors before making a decision. She advises primary care physicians to help educate families about the importance of research, and she reminds families that they should ask as many questions as necessary to make their decision, and that, in the end, they can say no.

Amy Billett '84, an HMS associate professor of pediatrics, says she is meticulous about informing families and patients about the differences between standard-of-care treatment and clinical research. Billett, who is also director of safety and quality for Dana-Farber/Boston Children's Cancer and Blood Disorders Center, has seen prospects improve dramatically for children with certain forms

of cancer. In some of the blood cancers, for example, cure rates exceed 90 percent.

Research now focuses on tuning treatment approaches to spare patients from troubling side effects. Billett is involved in a study testing a new form of a drug that has long been approved for therapeutic use. The aim is to determine whether the new form—which would be given every three weeks instead of every two weeks—works as well as the approved form of the drug.

Billett explains to parents that the researchers have no reason to think the new form of the drug is different from the old form. She also points out that researchers can't guarantee that the drug, if different, isn't different in a harmful way.

Leslie Lehrmann, an HMS assistant professor of pediatrics and the clinical director of the Pediatric Stem Cell Transplant Center at Dana-Farber/Boston Children's, encourages families to get a second opinion. She also stresses the broader importance of rigorously studying treatments.

"The beauty of a trial is that you're able to capture the path of every patient: the good, the bad, and the complications," she says. "In children, we are so focused on decreasing toxicity to allow them a normal lifespan that we conduct a trial to make sure that our thought that this is a gentler, safer therapy is really true."

When standard treatments fail, however, the risk of trying an experimental treatment may be more acceptable.

For the parents of a five-year-old girl with multiple malignant brain tumors, no decision has been easy. When chemotherapy failed, options seemed bleak. Then molecular analysis revealed that the tumor cells of her rare, incur-

able cancer carried a mutation in the *BRAF* gene that is found in 5 percent of such cancers. An experimental drug that blocks that mutation has been used extensively in adults, but never for brain tumors—and never in children.

Pediatric neuro-oncologist Mark Kieran, an HMS associate professor of pediatrics and the clinical director of the Pediatric Brain Tumor Program at Dana-Farber/Boston Children's, asked the young girl's parents whether they wanted her to participate in a clinical trial.

"As you break down each individual's tumor, it's almost like each trial is a unique trial for a unique patient," he says. "This child's tumor turned out to have a mutation identical to one found in an adult tumor, one for which pharmaceutical companies have already developed a drug. We're not always that lucky."

Knowing their child would be the first to receive this therapeutic approach unnerved the girl's parents. But that statistic was nowhere near as chilling as the statistics on her chance for surviving the cancer. After two months of treatment, her tumors disappeared. Now after nearly two years of taking pills twice daily, she is thriving at school and play, wearing sparkly outfits, and planning fishing trips.

Occasionally, there isn't even a faint hope of cure or prolonged life. In those situations, parents—and sometimes children—are motivated by the thought that their actions could help other children. In these cases, it is not therapeutic misconception that motivates participation. It is altruism. ■

Elizabeth Cooney is a science writer in the HMS Office of Communications and External Relations.



As funding for research wanes,

Running on Empty?

worries grow over the sustainability of the nation's scientific enterprise

Many physicians can recall the period more than three decades ago when a plague emerged that appeared to selectively afflict urban men. As death tolls mounted, no one knew why the immune systems of these patients deteriorated, how to treat the illness, or how widespread the sickness might become. ■ Thirty-five years have passed, and today, in most developed countries, people don't die of AIDS. Rather, they live with HIV. The same disease that was a death sentence in the 1980s had become a chronic condition by the mid-1990s. For the bench-to-bedside trajectory, this is light speed. Although pressure from patient advocacy groups certainly played a transformative role in the development and distribution of therapeutics, years of curiosity-driven, publicly funded basic research into retroviruses—organisms that were considered irrelevant to humans—had been aggregating a reserve of knowledge that spurred rapid and effective translational research.

by David Cameron

This is not an isolated anecdote.

Treatments for chronic myeloid leukemia, multiple myeloma, and even high cholesterol provide other examples of life-saving drugs that began at the bench during searches for answers to basic science questions.

The United States has been the world leader in cultivating a spectacularly successful culture of basic science, one that forms the bedrock of modern medicine. Support from such entities as the National Institutes of Health and the National Science Foundation has, on average, accounted for more than 50 percent of the global total of governmental investment in science. Likewise, the U.S. share of life-science patents worldwide exceeds 50 percent, despite a slight decline throughout the past thirty years.

During the past decade, however, there has been a slow, steady decline in public funding for research, particularly in the life sciences. And that is not going unnoticed. In fact, it is raising eyebrows, even alarm, among senior scientists, junior scientists, and other members of the scientific enterprise. The difficulty is not in identifying the problem, it's in constructing a solution.

The Numbers Game

Just look at the data. From 1994 to 2004, the NIH budget doubled from 17.6 to 35.6 billion, an average annual growth rate of 7.3 percent. From 2004 to 2012, however, the budget dipped to 30.9 billion, a negative growth rate of nearly 2 percent. Declines, in fact, appear to be the new normal.

In addition, there is an emerging sense that the scientific enterprise itself is caught in a kind of straitjacket. Decreased funding has caused a ripple effect throughout the system, perhaps nowhere felt more keenly than downstream among graduate students and postdoctoral researchers who may be looking at an increasingly uncertain future.

It's probably safe to say that no one thinks public funding will return to pre-2004 levels. As a result, there is a growing realization among scientists that the enterprise itself

needs to change some of its entrenched cultural practices to avert not only a brain drain of young researchers but a potential slowdown of critical discoveries.

If the problem seems difficult, the solution is a Gordian knot.

Double Trouble

Alfred Sommer '67, dean emeritus of the Johns Hopkins Bloomberg School of Public Health, was attending a congressional luncheon in the early 1990s when the topic of discussion turned to the doubling of the NIH budget and whether institutions would be able to absorb such an infusion of support. Sommer recalls being uncharacteristically silent during much of the debate, until he could keep quiet no longer.

"I told them that doubling was not the big deal," he says. "We would have no trouble putting that money to work. The problem, I said, was going to be when the doubling stops. At that point we would hit a brick wall. This was not rocket science."

Not rocket science, but prophesy. With the exception of a momentary bump from the American Recovery and Reinvestment Act of 2009, public funding for the life sciences has been flat.

The problem is more than addition and subtraction. According to Marc Kirschner, the John Franklin Enders University Professor of Systems Biology at HMS and founding chair of the School's Department of Systems Biology, the change in support has put the scientific enterprise under tremendous stress. Kirschner has teamed up with Bruce Alberts, former editor of *Science* magazine; Shirley Tilghman, past president of Princeton University; and Harold Varmus, former director of the National Cancer Institute, to try to bring this issue into the forefront of public discourse. The group coauthored a perspective piece in *Proceedings of the National Academy of Sciences* in 2014 titled "Rescuing U.S. biomedical research from its systemic flaws." In scientific circles at least, the article caused a stir.

The authors state that, for better or for worse, we have built a system predicated on indefinite expansion. In fact, many universities and research institutions have created infrastructures, even salary structures, that depend on a steady flow of grant money. And what happens when an enterprise founded upon steady increase suddenly slams against steady decline?

"Diminished funding leads to a hyper-competition where science is getting less creative and more risk averse," says Kirschner. "The less risky an idea, the more likely it is to get funded; it's obvious and a sure bet. But it's the risky, nonintuitive ideas that have advanced science."

Adds Sommer, "The less money there is, the more conservative the grant approvers get. They will fund things that advance linear thinking by a couple of microns. They will not fund right-angle turns. And most major medical breakthroughs are right-angle turns."

Kirschner and company's perspective article does make some recommendations, such as making budgets from public funding agencies more predictable, rectifying the imbalance of a peer-review grant-approval system that prefers large projects over those that are more imaginative, and changing policies that inadvertently promote unsustainable growth. But even more so, their intention was, and still is, to instigate public debate—and in this at least they have been successful.

Future Tense

Among the more notable public discussions is one driven not by individuals with storied scientific careers, but by an ad hoc network of postdoctoral scientists and graduate students in the Boston area who represent not only HMS and its affiliated teaching hospitals but also Boston, Brandeis, and Tufts universities; MIT; and the Whitehead Institute. The group has coalesced into an organization called The Future of Research. Last October, it convened a conference that brought scientists from both industry and academia together to discuss the current state of the scientific enterprise and how its culture should adapt to new funding realities. At the heart of their concern is the knowledge that the scientific enterprise

"The less money there is, the more conservative the grant approvers get. They will fund things that advance linear thinking by a couple of microns. They will not fund right-angle turns. And most major medical breakthroughs are right-angle turns."

increasingly requires a pool of trainees—postdocs and grad students—that is an order of magnitude larger than the job prospects that await.

"This system looks less and less attractive to young scientists," says Jessica Polka, an HMS postdoc and a cofounder of The Future of Research. "We certainly don't want young scientists to be counseled to stay away because research is an unstable career choice."

"There is a general fear among postdocs about what comes next," adds Kristin Krukenberg, an HMS postdoc and a cofounder of the organization. "We're realizing that almost everyone has these same fears. Conversations among postdocs are less and less about science and more and more about the fear of not getting published or of not getting grants."

Such conversations would have been alien to the young Kirschner who, like many of his contemporaries, received his first major research grant in his late twenties and tenure in his early thirties. Today, approximately four decades after Kirschner began receiving support for his research, the median age at which scientists first receive an independent research grant is 42.

Last November the conference organizers published their own perspective piece, "Shaping the future of research: a perspective from junior scientists," in the online journal *F1000 Research*.

The authors, who include Polka and Krukenberg, write, "While scientists continue to advocate for increased funding, they must also create a scientific enterprise that is sustainable with the current resources." Some of their suggestions include greater involvement by junior scientists and other stakeholders in shaping reform, increased transparency regarding career options and outcomes, a system of greater accountability for the quality of training, and the development of a funding system that allows trainees to be more financially independent and, therefore, less tied to particular principal investigators.

As important as any of these recommendations is the willingness to broaden the conversation. In that sense, you can say *The Future of Research* has syndicated. Similar groups of concerned postdoctoral researchers are planning such public conversations in New York City, Chicago, and in the San Francisco Bay Area.

"If we really want to change the culture of science," says Krukenberg, "young scientists need to be made aware of problems in the system. They can change the culture from within."

Kirschner and his team are also broadening the conversation. Recently they held a meeting at the Howard Hughes Medical Institute that brought together presidents of universities, CEOs of drug companies, and heads of NIH institutes, as well as other leaders from academia and industry. Other universities around the country are starting to host symposia as well. In 2014, Kirschner, Tilghman, and Varmus met with the president's Council of Advisors on Science and Technology, which devoted most of its meeting to discussing the subject.

According to Kirschner, there is near unanimity on the notion that the scientific enterprise has the seeds of its own destruction baked into it. Although parts of the enterprise are healthy, other parts are less so; those unhealthy parts need immediate action before they get much worse.

"The situation is complex," says Kirschner, "but it's not politically complex. There's not a lot of opposition. It's just not clear yet how to move forward with all this."

A Tale of Two Worlds

While not exactly a voice of opposition, Gilbert Omenn '65, a professor at the University of Michigan Medical School and director of the university's Center for Computational Medicine and Bioinformatics, adds words of caution to any sense of alarm.

"I think this is a Dickensian best-of-times, worst-of-times dichotomy," he says. "Science has never been more exciting than it is today, with more knowledge and great technology platforms. The NIH still awards \$31 billion per year, and other federal and foundation sources supplement that investment."

As Omenn sees it, new opportunities are always emerging. He is wary of any tendency to measure the quality of investment in a particular area by how much we have historically invested in that same area. That, he says, is not the right measure: The focus should instead be on emerging opportunities and bold goals.

He also points out that, while the low percentage of grants funded is certainly discouraging, during the five years that the NIH budget doubled, the number of grants submitted also doubled.

"This 'woe is us' talk is overdone," he says. "True, it is competitive, and it is a struggle. Nevertheless, we should encourage bright young people who have a passion for discovery and for making a difference to go into biomedical research. There is much to be accomplished in medicine and public health and much benefit to be achieved for society."

Kirschner agrees that today's scientific tools are very powerful and that in some ways new science is easier than it's ever been. But he sees this as a cruel irony.

"Opportunities to investigate are deeper than ever, but the constraints on the system are worse than ever," he says.

In the meantime, as uncertainties continue to obscure the path forward, Sommer offers some tried-and-true advice.

"Write your representative in Congress," he says. ■

David Cameron is the director of science communications in the HMS Office of Communications and External Relations.

BACKSTORY

FROM THE COLLECTIONS AT HARVARD MEDICAL SCHOOL

FROM THE BANKS of the Charles River to the Amazon Basin, HMS explorers have long plumbed the depths of medical knowledge in service to global health.

S. Burt Wolbach, Class of 1903, left London for The Gambia and Senegal in 1911, embarking on an expedition to research diagnostic methods for human trypanosomiasis, or sleeping sickness, and to determine the incidence of the disease in the territory. This trip had its hardships. Wolbach wrote in a letter to H. C. Ernst, a professor of bacteriology at HMS, that the “dust ... is very trying, and it rises and gets into everything. It is like setting up a laboratory in the middle of a dusty Boston street.”

An expedition in 1924 to the upper Amazon, led by Alexander Hamilton Rice, Class of 1904, to research tropical diseases counted among its party George Cheever Shattuck, Class of 1905 and an assistant professor of tropical medicine at HMS. They traveled by canoe and contended with malaria, infected insect bites, and machete wounds. Later, Shattuck was also a co-leader on one of the Harvard African Expeditions that conducted a biological and medical survey of Liberia and the Belgian Congo.

—Susan Karcz

PICTURES FROM AN EXPEDITION:
African helmet mask, (clockwise from right) attributed to the Bobo culture of the Burkina Faso region and described as having a characteristic artifact of onchocerciasis (river blindness): a prominent subcutaneous swelling on the facial plane, from a collection donated by Eli and Carolyn Newberger. Eli Newberger is an HMS assistant professor of pediatrics at Boston Children's Hospital and served as a Peace Corps volunteer in Burkina Faso in the 1960s. Viscerotome, an instrument used to take histological samples from cadavers, donated by Thomas P. Monath '66. Pre-Columbian clay sculptures from a collection donated by Louis E. Wolfson, a Boston physician.

Viscerotome courtesy of the American Society of Tropical Medicine and Hygiene at the Francis A. Countway Library of Medicine's Center for the History of Medicine. All other objects courtesy of the Harvard Medical Library.





FIVE QUESTIONS

FOR JUDITH PALFREY



Advocating for children's health has long been an interest of yours. How did the spark for this ignite?

I think that roots come from your family, your parents, and what they believe in and teach you. My father was a physician in Baltimore, and my mother was a social worker for Helen Taussig, considered the founder of pediatric cardiology. Taussig was interested in rheumatic fever. Since the streptococcal disease spreads rapidly in overcrowded living quarters, Taussig and her colleagues were out on the streets working on a social approach to a health problem. This is the world I grew up in.

What helped you become an effective advocate, mentor, and clinician?

It helps if you love what you do, and I certainly do. I was told years ago by a wonderful mentor that I have an integrative mind. I believe he was right. I integrate all the moving parts of community medicine and advocacy projects. The teaching model I work with is built on the idea that one of the responsibilities of a mentor is to steer students around the walls that can separate them from their passion to serve and care. This approach involves teaching by example on the wards and in the clinic and developing young faculty to serve as mentors for the generations that follow.

What brought you into global health?

Like many, I've become increasingly aware that our world is getting closer and smaller, that we're global citizens. After I stepped down as the division chief at Boston Children's Hospital, I volunteered to start a global pediatrics program there. Eight years later, we have a program in place that offers pediatric residency training, fellowship training in global health, and partnership programs with providers in four host countries. A bright light is that, in every country, young people represent an enormous resource; they are excited and want to work to improve health and social conditions in their countries.

Professor, Global Health and Social Medicine, Harvard Medical School

Professor, Department of Social and Behavioral Sciences, Harvard T. H. Chan School of Public Health

T. Berry Brazelton Professor of Pediatrics, Boston Children's Hospital

What global program are you working on now?

I'm working with Recupera Chile. This is the ultimate community health program. We are working to rebuild three seaside towns devastated by the 2010 earthquake in that nation. As recently as 2013, people in these towns were still living in shelters. We are working with them in every way: physically, socially, economically, and culturally. We are working with children in a school program to help them love the sea after they've been traumatized by it. We've found that all people need a little support and encouragement to start businesses and rebuild their lives.

Complete this sentence: The one thing a pediatrician must do to positively affect a child's health is ...?

... to find the child's support systems. You may have to search for them, but believe that they are there. You will see horrible things sometimes; but find the supports and then encourage and foster them. And share the work with someone. I could do none of the work I do without help from many people, most notably my husband, Sean. We are in some ways the same person on the same mission.

—Susan Karcz

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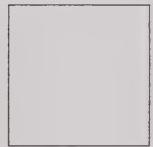
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THE COMMUNITY OF HARVARD MEDICAL SCHOOL ALUMNI

President's Report



A series of blizzards in February led to the cancellation of the Winter Alumni Council meeting in

Boston. We plan to make up for lost time in May. After reviewing alumni survey responses and talking with and receiving ideas from alumni through email, the Council decided that its emphasis this coming year should be on fostering greater alumni involvement in HMS. There will be five approaches to this. The first involves helping alumni get access to journals commonly used in medical practice. We encourage you to access them at hms.harvard.edu/alumni/lifelong-learning/online-resources. A second celebrates women at HMS, an effort that will underscore the upcoming seventy-fifth anniversary of the first cohort of women being accepted to HMS. Another approach involves local wine and cheese events, hosted by alumni throughout the country. In early March, Gil Omenn '65, and his wife, Martha, held the first such event in Ann Arbor, Michigan. These efforts will be complemented by two others: completing the class listservs so that class members can contact one another easily, and enhancing communication between the Office for Resource Development and donors.

Barbara McNeil '66 is the Ridley Watts Professor of Health Care Policy at HMS, founding head of the School's Department of Health Care Policy, and a professor of radiology at Brigham and Women's Hospital.



Alex Bick and Eran Hodis

THE 2015 FORBES "30 Under 30" lists include Alex Bick '16 and Eran Hodis '19, both students in the Harvard-MIT MD-PhD Program.

Bick was among the up-and-comers in the Forbes health care group because of his computer analyses of scientific and medical big data. His research showing how genetic mutations can affect a patient's response to blood pressure medication has been widely cited.

Hodis made Forbes' must-watch list in science for codiscovering genetic mutations that show how cancer cells increase the production of an enzyme that helps cells avoid natural death. These mutations in the genomes of melanoma cells are among the most common found in cancer cells.

Harvard Medicine asked each student to describe what went

into his decision to become a scientist and a medical doctor.

Alex Bick

"As MD-PhD students trained at HMS, we have a much better sense of what the interesting questions are.

"I truly love clinical work. If someday I'm the wonderful clinician I hope to be, I will be able to affect the lives of all the patients I see in clinic. That's a wonderful connection. But I would like to be able to help more than just the patients I care for. I feel that's where my work as a researcher will become important. Any doctor can repeat and use the results of research. That multiplies its impact and benefits many more patients than just my own."

Eran Hodis

"Before I moved back to Boston to be near a family member who had been diagnosed with cancer, I was interested in pur-

suing a PhD in science. There were two aspects of doing science that interested me. The first was to understand how the world works. The second was to do research that could have an impact on the world and possibly could lead to applications that would help cure or ameliorate disease.

"I knew I was interested in working on research that could eventually touch the lives of patients, but wondered whether I also wanted to work in medicine. I suddenly realized that both were okay; I could pursue research and take care of patients.

Within the scientific community, we aspire to inspire others. If in the future I'm fortunate enough to run my own lab and to have my own students, I'll be able to impart to them how to be a scientist in the hope that they will go on to make some important discovery that will help others." ■

CONNECT THE DOCS

THE COMMUNITY OF HARVARD MEDICAL SCHOOL ALUMNI



WORKING IT OUT

Krishna Yeshwant focuses on the business of being a doctor

STUDENTS AND FACULTY who come to HMS are understandably drawn to the vibrant educational and research community on the Quad and in the affiliate hospitals as they strive to improve health care delivery or gain insights into health and disease.

To have an even greater impact, says Krishna Yeshwant '09, they need to forge partnerships beyond Harvard's walls. That means reaching out to the business world that's flourishing just one email or T ride away.

Yeshwant, who earned an MD-MBA at Harvard, wants to encourage others to do just that. In September 2014, he was appointed special advisor on entrepreneurship to HMS Dean Jeffrey S. Flier.

"HMS has an amazingly talented group of people who are passionate about improving the system. They recognize that this is a rich ecosystem, but often don't know how to tap into it," says Yeshwant, an HMS instructor in medicine at Brigham and Women's

Hospital and a general partner at Google Ventures.

Yeshwant sees two main tasks in his advisory role: connecting HMS faculty and students with "the rest of the ecosystem here in Boston and across the country" and providing a context for what's possible when the worlds of medicine and entrepreneurship are combined.

It's no secret that medicine and biomedical research are undergoing rapid change, from the rise of sequencing and fabrication technologies to revisiting, even redefining, the doctor-patient interaction.

"Anytime you have such major shifts, there are a lot of entrepreneurial opportunities," says Yeshwant. "To take advantage of such opportunities, you need to connect with people who have the right skill sets."

Yeshwant is doing his part as an alumnus who has pursued an entrepreneurial career path and returned to HMS to serve as a role model for students and faculty. He wants to demonstrate to others that "there are many dimensions to what people can do with their skill sets after medical school."

"Alumni who straddle the line between health care and entrepreneurship may be among the first to recognize the next wave of innovation," he says. "Connecting them with other alumni will give them the support they need to go off and explore this flourishing sector."

The student body has already shown great interest. When students signed up for Yeshwant's office hours—on Fridays after his clinic appointments—two months' worth of slots filled in 15 minutes.

—Stephanie Dutchen

Ethics, Empathy, and Education

Albright Symposium honors student and spotlights advances in genetics and medical education

HOW CAN DOCTORS provide high quality, compassionate care to patients in low-resource settings despite technical and financial obstacles?

This and other questions exploring the bioethical concerns facing medical education, practice, and research were central to the 2015 Hollis L. Albright, MD '31 Symposium.

Held on March 4, "The Future of Medicine, Science and Technology" featured two keynote speakers and the presentation of the 2015 Albright Scholar Award to Shekinah Elmore '15.

Elmore has experience as both a medical student and a patient: She survived cancer at age seven; again, in her teens; and yet again two weeks before arriving at HMS. These experiences led her to write and speak about the importance of empathy in medical training. Her work has appeared in *JAMA*, *PLOS One*, and *BMJ's "Medical Humanities"* blog.

In addition to advocating for more compassionate cancer care, Elmore is dedicated to social



Shekinah Elmore

justice and global health equity. Her interests have taken her to Kenya, Malawi, Mozambique, Rwanda, and Uganda, where she has conducted award-winning research in such areas as palliative care and the provision of radiotherapy in resource-challenged environments.

Inequities exist at home as well, and Elmore has worked to improve quality of life for cancer patients and to better integrate compassionate care into medical training in the Boston area and across the United States.

In these ways and more, Elmore embodies Albright's belief that the patient should be at the center of medical practice, said symposium moderator George Daley '91, the

Samuel E. Lux, IV Professor of Hematology/Oncology at Boston Children's Hospital and an HMS professor of biological chemistry and molecular pharmacology.

"I think you'll agree this is a remarkable young person, whose life to date is really an inspiration to us all and who offers tremendous promise for the future," he said.

Elmore was unable to attend the symposium because she was working in Rwanda. She delivered a thank-you message by video.

"I'm luckier than many, but certainly not more deserving," she said. "I want to pay forward the advantages and access I've had."

—Stephanie Dutchen

CLASS NOTES

NEWS FROM ALUMNI



1945 70th REUNION

Giulio D'Angio

My wife, Audrey Evans, co-founded the first Ronald McDonald house in 1974. We have traveled far and wide for the 40th anniversary celebrations, including the United Kingdom, where we also attended medical meetings and Audrey's family celebrations.

I've been elected to honorary membership in three of the Societies I founded or co-founded years ago. These are the Histiocyte Society, the Society for Pediatric Radiology, and the Pediatric Radiation Oncology Society. Best part: no dues. I have also been recognized for distinguished service to pediat-

ric radiation and radiation oncology by the Society for Pediatric Oncology, the International Society of Pediatric Oncology, of which I am a past president, and the American Society for Therapeutic Radiation Oncology.

1947

Charles Lasley

I have retired after 60 years as a cardiac surgeon in Belleair, Florida. I have run twenty-five marathons and eighty-six triathlons. I still run six miles regularly on the Pinellas Trail, although I'm much slower at 93 years of age. I enjoyed visiting my friend and classmate John Stoeckle this year.

1948

J. Gordon Teter

I have retired after an enjoyable five years as general surgeon. Mary and I now live in a retirement community about 30 miles southeast of San Francisco. Greetings to all classmates.

1949

Raquel Cohen

Even though I have retired, last year I was inducted into the Peruvian American Medical Society National Academy of Medicine in Peru and named as one of the outstanding Latin leaders by the National Hispana

Leadership Institute Leaders. I also continue to consult on issues of mental health in natural disasters, trying to integrate physical and mental health into emergency training for humanitarian relief teams.

1955 60th REUNION

Charles Cahill, III

I am still practicing forensic psychiatry part-time. My last brief research paper was published in 2006.

1956

Robert Chamberlin

I have been volunteering with Healthy Start of Southwest Florida. We're working to connect home visiting programs for new moms with community-based family resource centers for all families with infants and young children in a defined geographic area. This approach has been working well in Vermont and New Hampshire.

1957

Wilbert Aronow

I received the 2014 Chancellor's Research Award from New York Medical College.

Harry Senger

In 2014 I joined the ranks of the retired. The timing was good, and I'm enjoying this stage of life, although it's hard to believe it has arrived.

1959

Gene Abrams

We have moved to a wonderful retirement community in Haverford, Pennsylvania. My book, *Living Right: The Ideal of a Moral-Spiritual*

Therapy, has been released by the self-publishing group iUniverse.

1963

Dale Cowan

I was awarded the 2014 Gold Medal by the American College of Legal Medicine at its annual meeting. Although I am semiretired, I continue seeing patients at the Siedman Cancer Center at University Hospitals Parma Medical Center in Parma, Oklahoma.

David Sachar

In the past year I received both the Suzanne B. Rosenthal Humanitarian Award and the Henry D. Janowitz Lifetime Achievement Award from the Crohn's and Colitis Foundation of America.

Andrew Warshaw

I've been installed as the 95th president of the American College of Surgeons, the largest surgical organization in the world. Its mission is to represent surgeons of all specialties nationally and internationally and to promote the quality of surgical care on behalf of patients worldwide. I'm also the W. Gerald Austen Distinguished Professor of Surgery at HMS and surgeon-in-chief emeritus at Massachusetts General Hospital.

1966

Dennis Bauman

I continue to work part-time in Elkin, a small town at the base of the Blue Ridge Mountains in north central North Carolina. This area is scenic and features a low cost of living, favorable climate, and a reasonable pace of life. I bike six and a half miles per day and enjoy my struggles with golf.

George Welsh

What a great class! I now work at five different clinics a week. Virtually the only qualification is to have a medical degree. On evenings and weekends I take riding lessons, compete at entry-level dressage and show jumping, and fox hunt in Kentucky. I edit our hunt newsletter. Hope to be at our 50th.

1967

Meryl Ram

Our son, Alan, has been married seven years and has two children. Our daughter, Lesley, married in 2013 and now has a baby girl. I retired from practice in 2013. Life is now very quiet!

here so as to concentrate on teaching, research, and patient care. My children, age 36 and 33, are in Durham, North Carolina, and doing well. HMS prepared me for a lifetime in medicine.

Stewart Gilbert

I recently retired after a successful career in internal medicine. In 2007, I completed a master of theology program and am now engaged in ministry. Travel and some volunteer work are on the agenda.

daughter, Amy, is a hospitalist in Memphis and our son, Eric, a computer scientist, lives in Tampa with our grandchildren Luke and Audrey. My wife, Eleanora, remains a treasure after 41 years.

Edmond Raker

I still love vascular and endovascular surgery. We have two grandchildren and two on the way.

1976

Laurie Green

Along with other HMS alumni, I'm actively involved in launching the MAVEN Project—the Medical Alumni Volunteer Expert Network. Joining forces with alumni of

1970 45th REUNION

Roger Barkin

I'm disappointed that I will miss our 45th reunion. Congratulations to all of our classmates. I continue to practice pediatric emergency medicine. Suky and I get tremendous joy from our two boys and their wives and our grandchildren. We continue to love living in Colorado and savor its beauty and available activities.

1973

Isaac Trimble, Jr.

Diana and I visited Portland, Oregon, in November, where Sandy and Steve Hohf entertained us in a grand manner.

1974

Christopher Baker

I am based at the Rush University. This year, I'm stepping down as Chair of Surgery at Carilion Clinic



CLASS NOTES

NEWS FROM ALUMNI



other medical schools, we are creating a national corps of volunteer physicians who use telemedicine to provide expert medical consultations to U.S. safety-net primary care providers. We need volunteers for our spring pilots in California and Massachusetts!

1977

Woodrow Myers, Jr.

I have spent the past year as the CEO of Corizon Health, the largest provider of health care services to correctional institutions in the United States. We focus on the universal adoption of electronic health records, comparative

health care analytics, and achieving reportable clinical outcomes (a somewhat different approach from that of the stereotype "jailhouse doc"). Our patients far too often receive the best health care of their lives once they are behind bars, and when they are released, they return to a system still too fragmented for many to navigate. I welcome collaboration with colleagues interested in the challenges of serving the underserved.

Camille Woodbury-Farina

I've retired from my private practice in psychiatry and am enjoying my two young grandchildren.

1982

Robert Lopez

Joanne (Moore) and I are still on the teaching faculty of New York-Presbyterian Hospital in New York City. I recently released "Hourglass," a new album of original songs.

Roger Macklis

I recently moved my practice and research program to the University Hospitals of Cleveland. I am still a professor at Case Western Reserve University, where one of our sons is applying to medical school.

1987

Emery Brown

In February, I became a member of the National Academy of Engineering, making me one of a small number of people who are members of all three branches of the National Academies—the Institute of Medicine, the National Academy of Sciences, and the National Academy of Engineering—and the first African American elected to all three.

1998

Abel Jarell

After serving in the U.S. Army, I'm now a civilian for the first time in more than 25 years. I have joined a dermatology practice in New Hampshire.

2006

Sachin Jain

I have been named chief medical officer of the CareMore Health System and am responsible for leading CareMore's care delivery, medical management, and clinical innovation activities. I'm thrilled to be joining CareMore as it is an example of what is needed in U.S. health care—better care for older adults and other vulnerable populations.

Share Your News

If you have updates you'd like to share in Class Notes, you can submit them easily and securely to classnotes@hms.harvard.edu. Be sure to include your full name and class year.

OBITUARIES

REMEMBERING DISTINGUISHED LIVES

1930s

1935

Arthur F. Toole
February 22, 2015

1939

Lewis S. Rathbun
April 11, 2015

1940s

1942

Richard W. Greene
March 2, 2015

1943

Donald G. Arnault
December 9, 2014

1944

Neill K. Weaver
January 13, 2015

1946

Murray E. Pendleton
February 5, 2015

Clifford J. Straehley
February 20, 2015

1947

Henry G. Carleton
December 12, 2014

Donal C. Edwards
February 15, 2015

Samuel S. Morrison
December 14, 2014

Richard A. Sanctuary
December 23, 2014

John J. Shea, Jr.
February 8, 2015

Kingsley M. Stevens
April 10, 2014

1948

David M. Gibson
January 20, 2015

1949

Louis F. Johnson
March 24, 2015

John D. States
March 26, 2015

1950s

1950

John O. Dampeer, Jr.
March 8, 2015

Dwight C. Hoeg
January 27, 2015

Feung B. Lee
March 19, 2015

1951

George B. Murphy, Jr.
December 11, 2014

Giles D. Toll
January 29, 2015

1952

Frederick J. Neher
March 13, 2015

1953

William W. Andrus
December 27, 2014

Harry B. Ditmore
February 22, 2015

John C. Herion
March 31, 2015

Calvin T. Hughes, Jr.
January 26, 2015

1954

William H. Loft
October 5, 2014

1959

Robert W. Carey
February 17, 2015

Lois B. Epstein
February 6, 2015

Irvin Taube
March 18, 2015

1960s

1960

R. Jackson Forcier
January 3, 2015

John M. Salzer
February 21, 2015

Robert T. Schaller, Jr.
December 7, 2014

Stephen L. Zaslow
February 19, 2015

1961

Frank O. Avantaggio, Jr.
February 8, 2015

Larry H. Strasburger
January 3, 2015

1962

Peter M. Gundersen
December 28, 2014

1963

James P. Keating
December 25, 2014

Jerry A. Tomlinson
November 29, 2014

1965

Philip E. Young
February 4, 2015

1966

Eugene L. Appel
March 7, 2015

1970s

1970

Mark R. Green
February 23, 2015

1971

Roger A. Rosenblatt
December 12, 2014

1990s

1993

Sara J. McCarthy
December 21, 2014

This listing of deceased alumni includes those alumni whose notices of death were received between December 13, 2014, and April 24, 2015. Links to full obituaries of these alumni can be found at hms.harvard.edu/memoriam.

If you know of an HMS alumna/us who has died recently, please send an email with the link to the obituary to hmsalum@hms.harvard.edu.

TAKING A HISTORY

PROFILE OF RISA LAVIZZO-MOUREY



CLAIMS TO FAME

President and CEO, Robert Wood Johnson Foundation

IN THEIR FOOTSTEPS

As a child, Risa Lavizzo-Mourey '79 would often accompany her parents, two of the five black doctors in Seattle, to work. "I got a feel for the exciting parts of medicine," she says. In middle school, she focused on her interest in becoming a physician and began working as a research assistant and learning more about science.

During her freshman year at the University of Washington, she filled out her class schedule with an introductory public health course. "That class," she says, "helped me see the world of public health and hear the language of medicine."

She vividly remembers her interactions with patients early in her medical training at HMS. "It was both grounding and exciting as I thought about the role of a physician in a person's life."

The enthusiasm she found among her peers at HMS was infectious. "It was thrilling to be with students whose aspirations were similar to mine." She recalls Match Day fondly. "Dean Tosteson told us 'you're all alumni,' and the mood was 'we've made it!'"

TWIN INTERESTS

While working as a primary care physician at Temple University Hospital, Lavizzo-Mourey says she began gravitating toward the complexities that geriatric medicine presented. At the same time, her interest in health policy grew. "I liked the idea of helping to improve the health of the general population," she says. "I felt that combining geriatrics with health policy would work for me."

Her involvement with policymaking increased and led to work with

White House health care task forces in the George H. W. Bush and Bill Clinton administrations and to co-chairing the Institute of Medicine committee assessing minority health care.

MOTIVATING FORCE

Her interest in policy drew her to the Robert Wood Johnson Foundation in 2001.

"Organizations like RWJF take a strategic approach to social change," which, she adds, is built on creative and innovative ideas. Since 2003, she has served as the foundation's CEO, a role that requires her to take the lead in shaping the organization's vision and strategy and to be the interface between the board, staff, and management.

A pivotal moment in her career as a nonprofit executive came in 2007 when RWJF announced a half-billion dollar commitment to reversing childhood obesity. "I was responsible for the vision, strategy, and implementation for making that bold statement." She was proud to get the board to support this dynamic new direction, despite knowing that the effort would be difficult to coordinate.

Lavizzo-Mourey says she finds inspiration in translating the foundation's work into action: "To see the impact on people's lives is a very motivating thing."

PATHS LESS FOLLOWED

When Lavizzo-Mourey isn't at the foundation or traveling in her role as CEO, she can often be found hiking.

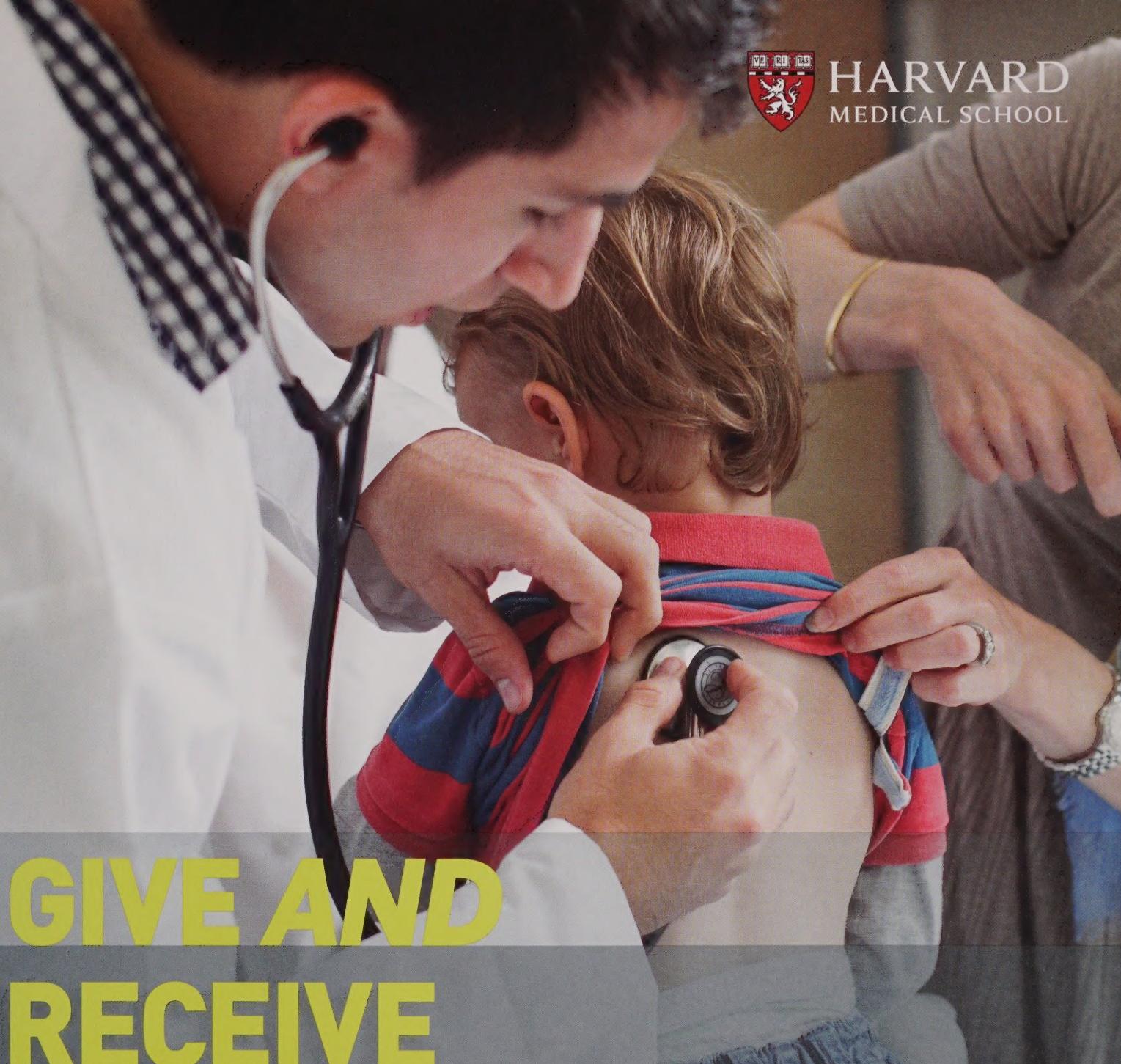
"I love to get outdoors and to enjoy the rhythm of the woods and my own footsteps." Her hikes are what she calls both routine and challenging, including her hike of Mount Kilimanjaro a few years ago.

"I also like to spend as much time as possible with my six-year-old granddaughter," she says.

—Katie DuBoff



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- The Future of Science: a podcast
- Match Day 2015: a photo gallery

